CONGENITAL ARTERIO-VENOUS FISTULAE

AND OTHER

VASCULAR ANOMALIES

BY

JAMES FLEMING CURR

M.B., Ch.B., F.R.C.S. Ed.

A Thesis Presented to the Faculty of Medicine
of the University of Edinburgh
for the Degree of Doctor of Medicine.

1945.

CONGENITAL ARTERIO-VENOUS FISTULAE

And Other VASCULAR ANOMALIES

SECTION ONE.

INTRODUCTION.

THE SCOPE OF THE INVESTIGATION.

The object of this thesis is to present an extensive survey of some rare congenital vascular anomalies, with special reference to arterio-venous fistulae. Interest was first aroused in those cases which showed a marked hypertrophy of a limb, along with numerous angiomata and varicose veins. Investigations revealed that these features had been described both in the presence and in the absence of arterio-venous fistulae, and, further, that arterio-venous fistulae could be found in the absence of hypertrophy or angiomata. Illustrating many of the varied and bizarre manifestations, a series of twelve cases has been examined and will now be reported, the presence of arterio-venous fistulae being found in nine cases, but not in the other three. These cases will, therefore, be described in considerable detail, along with brief reports on two other cases which have come to my notice.

Though the lesions under review are congenital, there has been much difference of opinion as to the underlying pathology, a haemangioma, indicating a true tumour, being maintained by some, and an actual maldevelopment of the vascular system being supported by others. Such opposing views are shown by the varied and confused nomenclature, the following being examples of names which might be applied to my own series of cases, and which have been freely used in the past:- arterio-venous aneurysm, anastomoses or fistulae; cirsoid or racemose aneurysm; aneurysm by anastomosis; aneurysmal varix; many varieties of haemangioma or naevus, such as cavernous, pulsating, plexiform, arterial or venous; haemangioma of bone or muscle; angiosarcoma; phlebarteriectasis; phlebectasis; cavernoma; haemangiectatic hypertrophy; hemihypertrophy; generalised angiomatosis.

There is, therefore, much to be gained by an attempt at simplification of the nomenclature; Craig and Horton (99), and Veal and McCord (57) believed that the majority of the cases of the type to be reviewed by me could be most easily included under the title of arterio-venous fistulae. It may perhaps be advisable to separate the vascular malformations into those with and those without arterio-venous fistulae, but Dean Lewis (41) admitted that clinically it was frequently /

frequently impossible to differentiate between the vascular lesions known as arterial racemose aneurysm and those known as diffuse phlebarteriectasis or phlebectasis. An added difficulty is that the term haemangioma has lost much of its original meaning and has become very loosely applied to lesions which are definitely not true neoplasms. In my presentation of the cases previously reported in the literature, I have not attempted to separate into different categories the various lesions described. A few obvious inconsistencies in the literature are here mentioned in support of my intention. The case described by Bockenheimer was quoted by Freund (56) as a genuine example of phlebectasis and yet it clearly was an example of arterio-venous fistulae with pulsation in the veins. Bland Sutton's (17) account of a case showed the features of definite arterio-venous fistulae and yet Davis & Kitlowski (13b) considered it a classical example of angioma of muscle. Lee and Freeman (89) gave excellent accounts of venous angiomata, but Homans (87), in discussing them, believed that small arterio-venous communications existed.

The field of investigation of these congenital vascular anomalies is so extensive that some restriction is necessary. There are in the review of the literature descriptions of arterio-venous fistulae, cirsoid aneurysms, diffuse phlebectasis, and haemangiectatic hypertrophy. The subject of haemangioma is a very large and separate problem and reference to it is chiefly concerned with its association with and relationship to the above, and with its development in muscle or bone. No attempt is made to classify any of the lesions as being in special tissues or in regions. The subject of lymphangioma is omitted and so also is hypertrophy of a limb, due to a cause other than a blood vascular condition. Intracranial vascular abnormalities and tumours are omitted, except for a brief reference to their association with the other lesions described. Also excluded are intrathoracic conditions such as arterio-venous fistulae in the lungs, communications between the coronary artery and sinus as noted by Halpert (113), and patent foramen ovale and ductus arteriosus. All intra-abdominal vascular lesions are excluded save those involving the iliac vessels, and all traumatic and acquired types in any situation are omitted. A discussion on glomangioma is given separately in Section Ten. My presentation of personal and past cases is thus carried out on similar lines to those of de Takats, Reid, Horton and his associates, and Dean Lewis, except for the exclusion of intracranial cases.

It was noted that some authors, as a result of their reviews of the literature, stated that a definite number of cases of a particular type had been previously/

previously reported. Almost all these statements were inaccurate and there is little to be gained by pointing out such errors. For example, Callander (114), Rienhoff (22), and Dean Lewis, among others, each stated specific numbers of such cases and yet closer scrutiny of British and American literature alone showed a much bigger figure. In reviewing the literature, therefore, I shall make no attempt to give an accurate figure, though mention will be made of more than three hundred and fifty cases.

PRELIMINARY ACCOUNT of the METHODS of EXAMINATION.

A full account will be given in Sections Four and Five of the methods of examination. Before presenting the personal cases, a brief indication is here given of the extent of these.

A complete routine clinical examination was made in all cases. Attention was directed particularly to the presence of haemangiomata, the presence of varicose veins and phleboliths, the consistency, size and function of the part, and the state of the local circulation. General cardiovascular effects were noted, such as variations in the pulse rate, and the blood pressure. Attention was directed to any disorder of the nervous system.

Certain special examinations were carried out in most cases. The estimation of the oxygen content of the venous blood was particularly important. Valuable information was obtained by straight X-Ray examination, angiography, skin temperature tests, and pathological examination. Numerous photographs were taken.

CASE 1.

D. McN. Male. Aged 17.

HISTORY.

Varicose veins of both lower limbs had been present since birth and there had been swelling of the left leg and ankle for many years. There was no history of phlebitis. The hands and feet, especially the digits, had been abnormally large, so that there was great difficulty in buying gloves which would fit. Numerous birth marks were present. The boy was intelligent and of good physical health. Until two years previously, he had played football but had had to give it up on account of the pain produced by any injury.

CLINICAL FEATURES.

Varicose Veins.

Left lower limb. A severe degree of varicose veins was present. The long saphenous vein formed a dilated, slightly tortuous trunk between the saphenous opening and the level of the medial condyle of the femur, at which level three large tributaries joined it. Following the course of these retrogradely, they appeared to pass from a very large plexus of veins which occupied the whole of the circumference of the leg and ankle region and part of the dorsum of the foot. The Trendelenberg test was positive, showing complete incompetence of the valves of the vein. Thus, with the veins emptied by elevating the limb, pressure was applied with the fingers over the saphenous opening, the patient stood up, and the superficial veins at first remained completely empty. However, slow filling took place about the level of the knee, showing the presence of an incompetent vein connecting the superficial and deep systems. On releasing the pressure, rapid filling of the veins took place from above downwards. The short saphenous vein was also incompetent and dilated. There was no evidence of previous phlebitis nor of the formation of phleboliths.

Right lower limb. The long saphenous vein in the thigh and the small saphenous vein were of normal size and quite competent. In the buttock at the inferior edge of gluteus maximus a large dilated incompetent vein, slightly tortuous, made its appearance. Above, it passed deeply, evidently to communicate with the inferior gluteal veins. Traced downwards, it passed /

passed behind the lateral condyles of the femur and tibia, on to the lateral side of the leg and had its origin from a small plexus of veins above the lateral malleolus. The Trendelenberg test was positive when applied to this vein. There was no evidence of previous phlebitis nor of formation of phleboliths.

The upper limbs and trunk showed no abnormal varicosities.

Angiomata.

In general, they were of the capillary type and superficial, but in the lower parts of the legs and feet, there was present more of the cavernous element. They were scattered widely and they took the form of irregular patches. They were of a mild reddish-purple colour in most situations and blanched on pressure with a watch glass. There were no apparent angiomata of the mucous membranes or the head. In no situation was there any pigmentation with melanin.

Left lower limb. The angiomata were scattered in diffuse patches throughout the leg, foot and toes. On the sole, however, there was one of a much deeper colour which was larger and broken only by a few small areas of normal skin. With the limb dependent, a diffuse dusky cyanosis was seen, making accurate delineation of the angiomata difficult.

Right lower limb. Smaller, irregular, brighter red angiomata were present on the dorsum of the foot and toes, excepting the great toe. A large angioma of deeper colour covered most of the sole.

Upper limbs. Patchy light red angiomata were scattered irregularly over the upper limbs from shoulder to fingers. The palms and palmar surfaces of the fingers showed a much deeper port wine discolouration, almost complete on the left hand and rather less on the right hand.

Neck, thorax and abdomen. In the middle of the back of the neck was a small angioma 1 inch in diameter. There were irregular extensive patches of angiomata on the upper posterior aspects of the shoulders and on the back of the thorax, the mid line of the back separating the two sides quite distinctly. At the root of the neck, there were small patches crossing the mid line, and on both pectoral regions, there were large patches which were separated distinctly by the midline. Below that level, the patches on the back were seen to extend laterally and forwards. Thus, on the right side they stopped abruptly at the mid axillary line, whereas on the left side, they were bounded /

bounded accurately by the mid line. The penis and scrotum were not affected.

Hypertrophy of the Limbs.

Hypertrophy was a striking feature, involving bone and soft tissue, but was uncommon in that all four limbs were involved, and in that it did not affect a limb uniformly. A preliminary glance showed the most obvious points to be the large size of the hands and feet, especially the digits, and the swelling of the left lower limb. There was no asymettry of the rest of the body. There was no impairment of function in any limb.

Upper limbs. The left upper limb was a little larger than the right in practically all measurements. On neither side did elevation or dependency affect the circumference. Both forearms were strongly developed and seemed large in comparison to the arms. An unusual feature was that the fourth finger was the largest on the left hand and as long as the right middle finger. The following were the principal measurements:-

Length.	Right.	Left.
Greater tuberosity - lateral epicondyle of humerus.	12 8/10 ins.	13 ins.
Tip of olecranon - ulnar styloid.	11 "	11½ "
Head of radius - radial styloid.	10½ "	11 "
Thumb.	3½ "	3 "
Index Finger.	4 3/10 "	4 3/10 "
Middle Finger.	4½ "	4½ "
Ring Finger.	4 3/10 "	4½ "
Little Finger.	3 "	3½ "
Circumference.		
Middle of arm	10½ ins.	11½ ins.
Forearm 2 inches below olecranon.	10½ "	11½ "
Forearm at level of head of ulna.	7 "	7½ "
Metacarpal heads.	9 8/10 "	10 1/10 "
Thumb.	3 7/10 "	3½ "
Index Finger.	3 8/10 "	3½ "
Middle Finger.	3½ "	3½ "
Ring Finger.	3 1/10 "	3½ "
Little Finger.	2 7/10 "	3 "

Lower /

Lower limbs. There was no difference in length but the left lower limb below the knee was of greater thickness. The toes were irregular in their size, the right second and the left second and third being very large. The left second and third toes were also partially webbed. The circumference of both limbs below the knee increased considerably on standing. The left foot was actually bigger but the large right second toe made the right foot longer. The following more important measurements were recorded:-

Length.	Right.	Left.
Anterior superior iliac spine - medial malleolus.	34 ins.	34 ins.
Foot.	10 "	$9\frac{1}{2}$ "
Toes - First	$2\frac{6}{10}$ "	$2\frac{7}{10}$ "
Second	$3\frac{2}{10}$ "	3 "
Third	$2\frac{1}{10}$ "	$2\frac{1}{2}$ "
Fourth	$1\frac{8}{10}$ "	2 "
Fifth	$1\frac{3}{10}$ "	$1\frac{8}{10}$ "

Circumferences.	Right.		Left.	
	Elevated.	Standing.	Elevated.	Standing.
Leg 4 inches below upper margin of tibia.	$12\frac{3}{4}$in.	13 in.	13 in.	14 in.
Leg immediately above malleoli.	$9\frac{3}{4}$in.	10 in.	$10\frac{3}{4}$in.	$11\frac{7}{8}$in.
Metatarsal heads.	$9\frac{7}{10}$in.		10 in.	

Local Circulatory Effects.

In no limb was there any evidence of impairment of blood supply, such as ulceration or gangrene. The arteries were normal and there was no pulsation, thrill nor bruit in relation to the veins. Little congestion of the upper limbs occurred on dependency. In the lower limbs, however, as noted in the measurements above, a considerable increase in the circumference of the legs took place on standing and the lower parts of the legs, the feet, and the toes became cyanosed.

An attempt was, therefore, made to estimate the volume of blood which passed into the angiomata and into the large veins, examining the two lower limbs consecutively. The limb was elevated in order to empty blood from the dilated veins, and a venous tourniquet was applied immediately above the knee, which had the effect of preventing the back flow of venous blood downwards into the leg, without constricting /

constricting the main arteries or the deep veins. The leg was then immersed in a tank of water, after which the tourniquet was removed. The superficial veins of the leg and the angiomata thereupon filled by the downward reflux of blood, which in so doing displaced a measured volume of the water in the tank. This volume of water displaced, therefore, indicated roughly the volume of blood which passed into the limb below the knee. One minute after release of the tourniquet, the measurement showed the displacement of water to be 240 c.c for the left leg and 30 c.c for the right. This test revealed the considerable loss of blood from the general circulation into the stagnant veins of the left leg, without even taking into account the extra loss into the veins of the thigh and knee which was not measured. The full significance of the test will be discussed subsequently.

General Cardio Vascular Effects.

The heart sounds were normal, and the pulse was regular and of a normal rhythm. The pulse rate, with the patient recumbent, was 60 per minute, whereas, after standing for one minute, it rose to 100 per minute. The blood pressure was the same measured in all four limbs, being 120/80 when recumbent, and 110/93 when standing. No bradycardia re-action could be elicited on pressure over the brachial or femoral arteries.

These various cardiovascular effects were of considerable interest. It appeared that, on standing, a large quantity of blood passed from the general circulation into the dilated veins and angiomata of the lower limbs so that it became relatively stagnant and lost to the general circulation. The resulting changes in pulse rate and blood pressure could, therefore, be likened to the effects of a moderate haemorrhage. The decrease in systolic pressure, the increase in diastolic pressure, and the decrease in pulse pressure were thus a protective mechanism compensating for the impaired cardiac return. Fainting, though not present in this case, has been reported as an additional feature (Lee and Freeman 1889), and was due to temporary poor cerebral circulation.

Negative Clinical Findings.

Pain was absent except that bruises produced by injury caused more discomfort than usual. The alimentary, respiratory and nervous systems were normal. Examination of the blood and the eyes showed no abnormality. The urine was normal.

SPECIAL/

SPECIAL EXAMINATION.

Oxygen Content of Venous Blood.

Blood was withdrawn from the veins of all limbs, using the recognised technique to be described later. Specimens from the forearms showed readings of 6.2 volumes % for the right side, and 7.5 volumes% for the left side. Several estimations were made of the blood from the lower limbs. Specimens from the right lower limb at different levels gave readings of 11.3 volumes %. A specimen taken from the left calf gave a reading of 11.4 volumes %, but that from the left thigh showed 13.0 volumes %. It was thus believed possible that a small degree of abnormal arterio-venous communication might exist in the thigh to account for this difference.

X-Ray Examination.

No abnormality could be detected in the skeleton, except for the changes obvious clinically. Arteriography and venography were not carried out.

Skin Temperature Tests.

The temperature of the feet was tested and the amount of possible reflex vasodilation also measured using the method of Landis and Gibbon. The feet were stabilised at a constant room temperature of 23°C and the terminals were attached to the second toe of each foot. The temperature was about ½°C higher on the left side. On immersion of the hands in water at 46°C, there was an immediate reflex vasodilation in the lower limbs producing a sharp rise in temperature, rather more marked on the left side. Thereafter, the temperature on the left side remained 1½°C higher than on the right. The response on both sides, however, was quite within normal limits. There was no special significance in the difference in temperature in the two lower limbs. The higher readings on the left side could be easily accounted for by the more marked venous congestion, though, on the other hand, they might be due to arterio-venous communications.

DIAGNOSIS.

A diagnosis was made of the syndrome of varicose veins, angiomata and osteohypertrophy. It was possible that small arterio-venous communications might exist in the left thigh.

TREATMENT.

It was evident that no treatment was necessary for the upper limbs or the trunk. In the lower limbs, the varicose veins alone needed treatment and, even if arterio-venous communications existed, no further measures would be called for. It was intended to treat both lower limbs, but unfortunately the left limb alone received treatment, as the patient finally discontinued attendance. The aim was to ligate the large incompetent veins and then to sclerose the remaining veins with injections.

At the first operation, using local anaesthesia, the left long saphenous vein was exposed at its upper end in the groin, and found to be very large. The vein was ligated and divided close to its entry into the femoral vein, a length of two inches was excised and the lower end was ligated. Two large tributaries were also ligated and divided. During the operation, a considerable amount of oozing of blood took place from small venous channels. Haemostasis was secured and the skin wound was sutured. Three days later, a fairly large haematoma had formed, necessitating opening of the wound to evacuate it. A mild degree of infection followed and healing was slow and not complete for over a month. Thereafter, fairly satisfactory thrombosis took place in the veins of the upper part of the thigh.

A second operation was carried out nine months later, a general anaesthetic being used. The left long saphenous vein was exposed in two places, at the middle of the thigh and at the level of the knee. At each site, numerous tributaries were ligated, a length of three inches of vein was excised and the proximal and distal ends were ligated. In the lower incision, in addition, injections of lithium salicylate 2 c.c and quinine urethane 2 c.c were ⊠ given into the distal end of the vein. ⊠ Elastoplast bandages were applied from toes to groin, over the sterile dressings. Thereafter, the boy rested in bed for ten days.

Seventeen days after this operation, the elastoplast bandages and dressings were removed, and, though the wounds were healthy, sound healing had not yet occurred and there was still a slight ooze of blood. Dressings and elastoplast bandages were re-applied for two weeks more, during which time oozing of blood continued. Thereafter the wounds healed soundly. Subsequently six injections of lithium salicylate were given at fortnightly intervals into the veins in the lower part of the leg.

⊠ (Lithium salicylate 35% and planocaine 1% in aqueous solution)

(Quinine hydrochloride Gm4 and urethane Gm2 in distilled water 30 c.cs).

SUBSEQUENT COURSE.

The result of the operations was to produce a considerable degree of thrombosis of the long saphenous vein at its tributaries in the regions of the thigh, knee and upper half of the leg. The veins in the lower half of the leg and around the ankle were now less marked, though still dilated. The injections of a sclerosing solution had thus produced a moderate amount of improvement and the limb became less swollen on standing. On measuring again the volume of blood which passed into the veins in the leg on release of a tourniquet, it was noted that only 100 c.c of water were displaced as against the 240 c.c before treatment. Another effect was that, on standing, the pulse rate was 90 per minute instead of 100 per minute as before.

PATHOLOGICAL EXAMINATION.

The segments of vein removed at operation showed the typical structure of a varicose vein, without valves. There was no other abnormality.

COMMENT.

As already stated, a diagnosis was made of the syndrome of varicose veins, angiomata and osteo-hypertrophy, which features have been described in some detail. Other important features were the cardiovascular effects, the oxygen content of the venous blood, and the long continued oozing from the operation wounds.

Much has been written in the past of cases showing the above syndrome, the earliest reference traced being in 1856. In spite of being known for so long, the reports were largely descriptive, with little information on the underlying pathology. Perhaps the most important result of study of previous reports was that these three features had been described by some as a separate entity and by others as forming the prominent features of arterio-venous fistulae. It was generally agreed, that these three main features were due to some fundamental error and were not associated merely by coincidence.

The nomenclature applied to cases like the one under discussion has been varied and confusing, and many names have been applied, in addition to the mere descriptive title of the syndrome. It was believed that there was a congenital abnormality of the veins so that they were varicose at birth or became so/

so soon afterwards. The angiomata were probably further evidence of a vascular abnormality and appeared to be filled with blood directly from the varicose vein, so that the term venous angiomata was common. Alternatively, the term phlebectasis might be used, indicating the extensive venous dilatation found in the more widespread lesions. With more emphasis on the osteohypertrophy, the terms haemangiectatic hypertrophy or hemihypertrophy have been applied to cases where one or both limbs on the same side, or rarely on opposite sides, were enlarged; in my own case, the left upper and lower limbs were enlarged in comparison with the right. The terms "syndrome of Klippel and Trenaunay", "naevus variqueux osteohypertrophique" and "syndrome of Parkes Weber" have also been in use. It was thus noted that any of the terms mentioned above could be aptly applied as the diagnosis of my case.

Among the many writers on the subject previous to the last twenty years, Telford (1912)(16) may be quoted. His case showed hypertrophy, angiomata and varicose veins, but the cause was admitted to be unknown.

The most complete recent description of the syndrome was given by Lee and Freeman (1940)(89)who described three cases, quoted more fully later, which had a strong resemblance to the case in question. In all there were varicose veins, angiomata and osteohypertrophy of congenital origin and affecting the lower limbs. There was no evidence in any of arteriovenous fistulae as shown by a normal oxygen content of the venous blood, even although, in one case, it was collected from the femoral vein. The interesting points of similarity were numerous. In Case 2 of their series, for example, the angiomata and varicose veins affected one lower limb, whereas there was hypertrophy of both feet, especially certain toes, and in Case 3 there was hypertrophy of the bones of both feet and one upper limb. In Case 2 also, the prominent varicose vein was in an abnormal situation, with its upper end communicating with the gluteal veins in the buttock. In Cases 1 and 3, there was a marked increase in the volume of the leg on release of a tourniquet. Cardiovascular signs were prominent on standing from a recumbent position, e.g. in Case 1 the blood pressure fell from 135/85 to 90/70, and the pulse rate increased from 60 to 152. The effects of operation were similar in their general and local effects, and the same slow healing of wounds and the long continued oozing of blood took place. My own case did differ from these or any other recorded cases in that all four limbs showed evidence of the abnormality.

Other /

Other good references to allied cases are those of De Takats (1932)(51) and Reid (1931)(76). Reid's case was diagnosed as a venous angioma but was peculiar in that the affected limb was shorter than the normal.

Homans (86)(87) described a case of venous angioma of the lower limb. He was of the opinion, thus differing from Lee and Freeman, that in such cases nearly always an important arterial connection of some sort will be found.

Veal and McCord (1936)(57) demonstrated the presence of arterio-venous fistulae in cases showing varicose veins, angiomata and osteohypertrophy, which would otherwise have been considered as venous angiomata. Arteriography and their special method of collecting specimens of blood for the oxygen content test were the methods on which they relied.

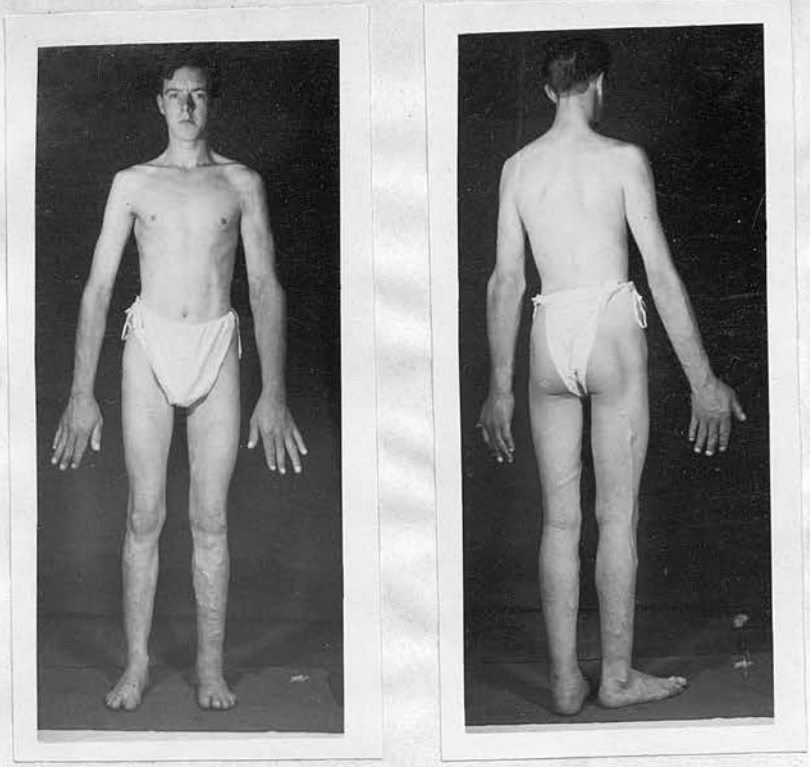
Horton and his associates (98)(99) also believed that almost all cases showing the syndrome must have been associated with arterio-venous fistulae.

There were thus difficulties in arriving at an accurate diagnosis in my case. There was certainly no evidence of arterio-venous communications in the upper limbs or in the right lower limb, and one might justifiably give the name of venous angioma to these lesions, with the reservation that a vascular abnormality rather than a true tumour was present. The condition of the left lower limb might evoke more discussion. In almost all its features, it corresponded to the description by Lee and Freeman of venous angioma, but the one critical point was the significance of the reading of the oxygen content of the venous blood. As mentioned, in the calf this was 11.4 volumes % and in the thigh 13.0 volumes %. Neither was an abnormally high figure but by some authorities the difference would be considered important, indicating that a small amount of arterial blood was entering the great saphenous vein in the thigh. It was not likely that the difference could be due to technical errors, as repeated examinations in this and in other patients were always known to give the same results. The absence of abnormal pulsations, thrill or bruit was accepted as not being of essential diagnostic importance. It was concluded that a very small degree of arterio-venous communication existed in the left thigh.

The ultimate prognosis should be satisfactory. It is most unlikely that any disability will arise in the lesions of the trunk and upper limbs. It /

It is possible that ulceration of the toes and legs may develop and there is even the slight risk of gangrene of the toes or feet. Another risk, which will be described fully in connection with other cases, is that unexpected lesions may be present in the viscera, particularly the brain and spinal cord.

To summarise, therefore, this was a case showing (1) the syndrome of widespread angiomata, irregular osteohypertrophy and varicose veins of the lower limbs; (2) left hemihypertrophy; (3) venous angiomata and probable arterio-venous fistulae.



Figs. 1 & 2, Case 1. Large size of both hands, and certain fingers, especially left fourth; increase in size of left upper and lower limbs; prominent varicose veins in both lower limbs, including anomalous vein in right thigh.

Fig. 3, Case 1. Increased size of left leg and foot and of several toes on both sides; slight webbing of left second and third toes; prominent varicose veins; patchy discolouration due to haemangiomata.

Figs. 4 & 5, Case 1. Irregular hypertrophy of fingers; patchy discolouration due to haemangiomata.

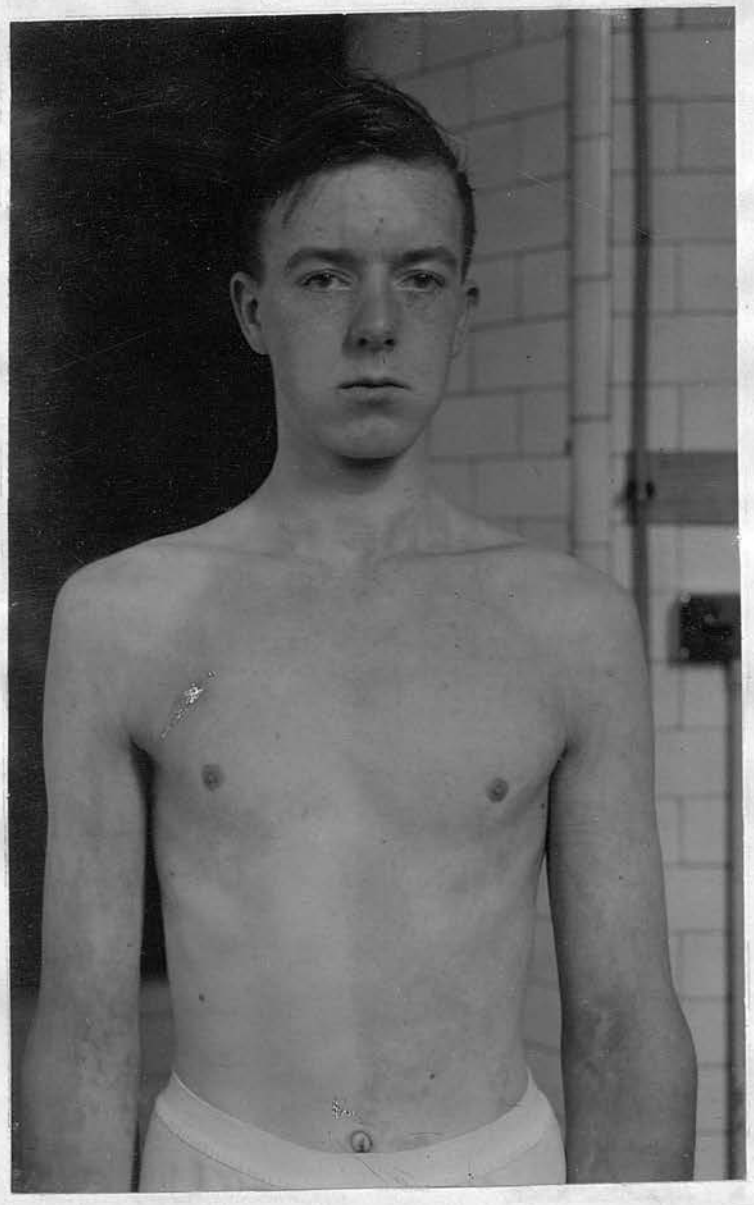


Fig. 6, Case 1. Widespread distribution of haemangiomata, with strict line of demarcation in mid line of anterior abdominal wall.

CASE 2.

Mrs. R. Aged 50.

HISTORY.

The patient was admitted to hospital on April 2nd, 1938, having been involved in a street accident. An obvious fracture of the shaft of the right femur was present and preliminary treatment consisted in the application of a Thomas' splint and extension by means of adhesive strapping. X-Ray examination, carried out immediately, showed the fracture of the middle of the shaft of the femur, with 2 inches of overlapping of the fragments, and it also revealed pathological changes to be described subsequently.

The past history was of interest. The patient stated that the right lower limb had been weak, but of increased girth, for as long as she could remember, and that she had always walked with a limp. Otherwise she was very healthy and had three strongly built sons.

CLINICAL FEATURES.

The usual features of a traumatic fracture of the shaft of the right femur were present, but routine examination revealed certain abnormalities which were not associated with the accident. The entire right lower limb, from the region of the hip to the foot, was the site of multiple, diffuse venous dilatations, some of which were $\frac{1}{4}$inch to $\frac{1}{2}$inch in diameter, whereas the majority took the form of telangiectases and spider marks. These veins were slightly compressible; no abnormal pulsation was present in them nor any bruit nor thrill. There was no obvious enlargement of the long or short saphenous veins. A generalised bluish discoloration was present over the whole limb. The left lower limb was normal.

After correction of the shortening and deformity due to the fracture, no difference in length of the lower limbs could be detected. Measurements of the circumference of the thigh were naturally difficult to estimate, on account of the swelling at the site of fracture. However, three weeks after admission, it was noted that the circumference of the right thigh was still greater than that of the left thigh at corresponding levels; for example, in the middle third of the thigh, there was an increase of $1\frac{1}{2}$ inches. Similarly, the right leg showed an increase /

increase in circumference of 1 inch at the level of the thickest part of the calf. The feet were of equal size. There was no obvious difference in temperature between the two limbs.

Routine general examination of the patient revealed no abnormalities elsewhere; in particular, no pathological cardio-vascular or nervous signs were present.

X-RAY EXAMINATION.

The fracture of the femur was of a commonly recognised type, being oblique and situated immediately below the middle of the shaft. The upper end of the lower fragment was displaced backwards and upwards, producing two inches of shortening and considerable deformity. Satisfactory position of the fragments, however, was obtained by treatment carried out soon after the accident.

Of greater interest than the actual fracture were the pathological changes unexpectedly encountered and obviously of long standing. Marked bowing of the femur towards the lateral side was apparent and there was generalised atrophy of the bone, producing a definite decrease in its girth. The bony trabeculae were irregular in their distribution and enclosed multiple rarified areas, so that almost the whole bone appeared to be the site of multiple small cysts. Many phleboliths were present in the soft tissues, forming small rounded opacities scattered between the iliac crest and the lower end of the femur; these were not palpable clinically. The soft tissue shadow showed an increased thickness of the thigh. X-Ray examination of the leg and foot was not carried out.

TREATMENT.

The essential treatment was the immediate care of the fracture of the femur. Two days after admission, the method of traction on the limb by adhesive strapping was replaced by skeletal traction, using a Kirschner wire inserted through the lower end of the femur. A Braun's splint was used instead of the Thomas' splint, and X-Ray examination thereafter indicated a satisfactory position of the fragments, without over-riding and without unnecessary distraction. No treatment was attempted for the venous abnormality.

SUBSEQUENT COURSE.

In spite of adequate surgical care, union of

the fracture unfortunately did not take place, as, even 3½ months after the injury, practically no callus had formed. Open operation, with a view to plating the fracture, was contraindicated, owing to the technical difficulties presented by the vascular abnormality of the soft tissues and the bone atrophy. An ischial bearing Thomas' splint, with leather corset fitting round the thigh and allowing knee movements, was therefore fitted. The patient was able to walk well with this almost at once and left hospital five months after admission. Reports recently received about her condition showed that no sign of bony union was present but that she was able to walk without difficulty, wearing the splint.

COMMENT.

The most prominent features in this case were the gross degree of venous dilatation of the affected limb, the pathological changes in the femur, the un-united fracture and the large numbers of phleboliths. It was certain, therefore, that the lesion was widespread and involved skin, subcutaneous tissues, muscle and bone.

Purely clinical observation suggested the diagnosis of diffuse phlebectasis or the synonymous term venous angioma. The abnormality appeared to affect the veins only and there was no obvious evidence of arterio-venous fistulae, such as pulsation in the veins, a thrill or a bruit. It was unfortunate that the oxygen content of the venous blood was not tested, as it would have shown definitely the absence or presence of abnormal arterio-venous communications. This was unavoidable at the time the patient was examined as the full significance of the test was not then appreciated, and as I was not in charge of the investigations and treatment. While most probable, therefore, that the condition was a phlebectasis, the presence of several small arterio-venous fistulae could not be ruled out. The phleboliths also showed the widespread nature of the vascular abnormality but were not diagnostic of its type. The case, therefore, showed many of the features which have been described as typical of phlebectasis but there was a strong resemblance to Cases 6, 7 and 8 of my series in which arterio-venous fistulae were present. Other interesting points were the absence of any superficial capillary angiomata and the absence of any increase in length of the limb.

The bony condition, as shown by X-Ray examination, was a rare one, and it was possible that it had no particular relationship to the lesion of the soft parts. The bowing of the femur certainly suggested that it was of no recent onset. An atypical, localised

form /

form of osteitis fibrosa cystica might have accounted for the bowing, the atrophy and the irregular cystic appearance, but the eppearances and the congenital origin did not support this. Osteitis deformans, while able to produce the bowing, would have given rise to thickening, and sclerosis of the bone, and also changes in the opposite limb. There was no feature to suggest rickets, osteomyelitis, tuberculosis, syphilis or malignant bone tumours. It was, therefore, thought that the bony condition was undoubtedly associated with the soft tissue lesion and was what is loosely termed a haemangioma of bone. This term, however, covers various types. A localised lesion, an actual tumour according to some, may occur in the presence of a soft tissue vascular abnormality or may arise alone. A widespread lesion, occupying the whole of one or more bones, is likewise known as an angioma, indicating a tumour. Another variety of lesion is that in which the one or more affected bones are riddled with multiple vascular channels, either carrying venous or arterial blood. This last explanation is by far the most likely in the present case.

There were numerous references in the literature to cases of phlebectasis or venous angiomata, not necessarily associated with increase in length of a limb or cutaneous angiomata. There was less mention of cases of phlebectasis, or vascular anomalies not obviously due to arterio-venous fistulae, in which pathological bone changes were present. Lereboullet and Petit, cited by Parkes Weber in 1918 (116), described in 1914 a case of congenital varicose veins of an upper limb, with fragility of the bones and ununited fracture of the forearm. Couch in 1935 (53) gave an account of a case of haemangioma of the upper limb, with phleboliths and frail irregular bones, which became fractured but united. Nemenov in 1939 (83) reported a case of angioma of the radius and ulna with previous fractures and with a vascular anomaly of the soft parts. Kleinberg in 1942 (104) treated a case of angioma of the foot, in which the soft tissues were involved and a destructive cystic lesion of the tarsal bones existed; at operation a free communication of vessels was found between the soft tissues and the bone. However, a full account of such bony lesions is given in a later section.

To summarise, a report is given of a case of diffuse phlebectasis of a lower limb, in which the presence or absence of small arterio-venous communications could not be determined.

Fig. 9, Case 2. X-Ray film - fracture of shaft of femur; atrophy and bowing of femur; numerous phleboliths.

Fig. 10, Case 2. X-Ray film - non-union of fracture five months after injury.

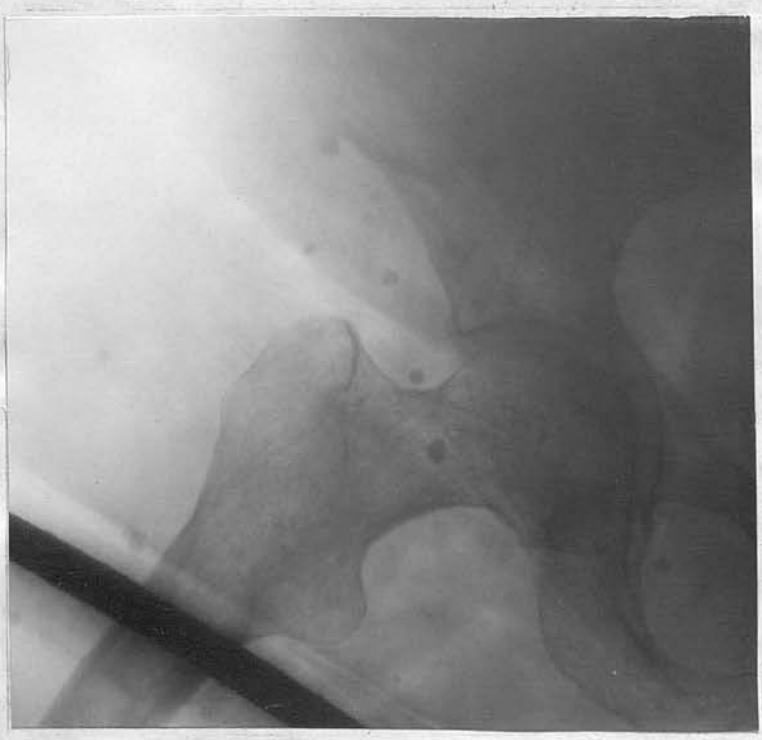


Fig. 11, Case 2. X-Ray film - phleboliths in region of hip.

CASE 3.

W. M. Male Aged 13.

HISTORY.

Immediately after birth, it was noted that the left lower limb was larger than the right, and that it was the site of many birthmarks. A few years later, several enlarged veins became prominent in that limb. The limb had never given rise to disability and, in spite of its large size, the boy was able to play football. Pain had never been present. There was no family history of similar deformities.

CLINICAL FEATURES.

Angiomata.

The entire left lower limb was diffusely involved in haemangiomata. There was one enormous dull bluish angioma, of the capillary or superficial type, over the buttock and posterior surface of the thigh. Numerous other angiomata of a similar appearance were scattered in irregular patches over the thigh, knee and leg. On the foot were several more discrete, smaller angiomata of a lighter red colour. The colour of all these blanched on pressure with a watch glass and it became more marked and the lesion tense on standing. There was no abnormal pigmentation with melanin. No angiomata were present elsewhere.

Hypertrophy of the Left Lower Limb.

A marked degree of hypertrophy of the left lower limb was present, both in length and girth. On standing, the pelvis tilted considerably owing to the inequality of the limbs and scoliosis was produced. The position of comfort therefore assumed when erect was usually with the hip and knee slightly flexed. The entire limb from buttock to toes showed increase in size fairly uniformly, as shown by measurements, but most noticeably in the leg. The function of the limb was in no way disturbed, and the consistence was quite normal. The following were the most important measurements:-

Length. Anterior superior iliac spine - adductor tubercle.

R. 16 3/10 ins. L. 17 1/10 ins.

Anterior/

Anterior superior iliac spine - medial malleolus.

R. 28 ins. L. 31 ins.

Circumference. At upper edge of patella.

R. 12 ins. L. 14 ins.

At upper end of tibia.

R. 10 3/10 ins. L. 11 6/10 ins.

Above malleoli.

R. 7½ ins. L. 9 ins.

Varicose Veins.

Varicose veins, showing moderate dilatation and tortuosity, were noticeable on the lateral side of the left thigh, knee, leg and dorsum of foot. They appeared to communicate with veins in the buttock, and a positive Trendelenberg test could be elicited on pressure at the lower edge of gluteus maximus. When recumbent, the veins were soft and compressible, but on standing they became full, tense and prominent, thus increasing the circumference of the limb. This enlarged incompetent venous trunk was an anomalous one, and there was no abnormality of the long and short saphenous veins. No dilated veins were present in the other lower limb or elsewhere.

Local Circulatory Effects.

As regards the local circulation in the limb, there was evidence of an increased blood supply. The entire limb felt hotter to the touch and mention of this will be made in detail later. The circulation, especially in the toes, was satisfactory, and there was no evidence of sores or ulcers at any point. As mentioned, the veins became greatly engorged on standing, producing an increase in the circumference of the limb especially in the region of the ankle. No abnormal pulsation, no thrill nor any bruit was elicited in the veins or arteries. Examination of the pulses showed that the subclavian, brachial and radial were equal on the two sides, but that there was a definite increased volume in the femoral, popliteal, dorsalis pedis and posterior tibial of the left side in comparison to the right.

General Cardio-Vascular Effects.

Blood pressure readings were as follows:- brachial artery both sides 130/80; right femoral artery 140/90; left femoral artery 158/105. Changes were /

Anterior superior iliac spine - medial malleolus.

R. 28 ins. L. 31 ins.

Circumference. At upper edge of patella.

R. 12 ins. L. 14 ins.

At upper end of tibia.

R. 10 3/10 ins. L. 11 6/10 ins.

Above malleoli.

R. 7½ ins. L. 9 ins.

Varicose Veins.

Varicose veins, showing moderate dilatation and tortuosity, were noticeable on the lateral side of the left thigh, knee, leg and dorsum of foot. They appeared to communicate with veins in the buttock, and a positive Trendelenberg test could be elicited on pressure at the lower edge of gluteus maximus. When recumbent, the veins were soft and compressible, but on standing they became full, tense and prominent, thus increasing the circumference of the limb. This enlarged incompetent venous trunk was an anomalous one, and there was no abnormality of the long and short saphenous veins. No dilated veins were present in the other lower limb or elsewhere.

Local Circulatory Effects.

As regards the local circulation in the limb, there was evidence of an increased blood supply. The entire limb felt hotter to the touch and mention of this will be made in detail later. The circulation, especially in the toes, was satisfactory, and there was no evidence of sores or ulcers at any point. As mentioned, the veins became greatly engorged on standing, producing an increase in the circumference of the limb especially in the region of the ankle. No abnormal pulsation, no thrill nor any bruit was elicited in the veins or arteries. Examination of the pulses showed that the subclavian, brachial and radial were equal on the two sides, but that there was a definite increased volume in the femoral, popliteal, dorsalis pedis and posterior tibial of the left side in comparison to the right.

General Cardio-Vascular Effects.

Blood pressure readings were as follows:- brachial artery both sides 130/80; right femoral artery 140/90; left femoral artery 158/105. Changes were /

were noted in the behaviour of the pulse rate; when recumbent it was 60, when standing 80 per minute. No bradycardia reaction was elicited on compression of the femoral artery. No cardiac lesion was noted.

SPECIAL EXAMINATIONS.

Skin Temperature Tests.

Accurate measurements of the temperature were obtained, using an electric galvanometer.

The first test consisted in recording the temperature at several corresponding levels on the anterior surfaces of the lower limbs, at a constant average room temperature of 15°C.

These readings were as follows:-

	Right.	Left.
Mid thigh.	28.0°C	29.5°C
Middle of tibia.	26.0	28.0
Medial Malleolus.	23.0	27.0
Dorsum of foot.	23.5	25.0
Great toe.	20.0	19.5

The second test consisted in comparing the degree of vaso-dilatation in the two lower limbs in response to heating of the hands, readings being taken from the great toes. On immersion of the hands in water at 43°C, there was a pronounced, though rather slow, vaso-dilatation, with the temperature on the left side remaining 1-2°C higher, and with a more rapid response on that side.

Oxygen Content of Venous Blood.

This test revealed very instructive changes and gave positive evidence of the presence of abnormal arterio-venous communications in the left lower limb. Blood was collected from veins at corresponding levels of the two legs, using the usual technique, and the readings were:- R. leg 9.2 volumes %; L. leg 18.6 volumes %. After operation, a dramatic change was noted as the reading for the L. leg dropped to 9.3 volumes %, thereby indicating the successful closure of fistulous communications between arteries and veins.

Straight X-Ray Examination.

X-Ray /

X-Ray examination of the two lower limbs, taken simultaneously on the same film showed the very striking increase in length and girth of the left side, particularly in the bones of the leg. The actual structure of the bones was in no way abnormal, except for the following outstanding change. In the lower quarter of the diaphysis of the femur, stopping abruptly at the epiphyseal cartilage and involving most of the thickness of the bone, there was an area of very marked rarefaction, with thinning of the centre, and thin, irregular, bony trabeculae, giving the appearance of many small cysts. It was believed that this lesion was an angioma of bone on account of its coincidence with the vascular lesion in the soft parts. There was no formation of phleboliths in the soft tissues.

Arteriography.

Professor J.R. Learmonth carried out this investigation by exposing the upper end of the left femoral artery through a transverse incision slightly distal to the inguinal ligament, a general anaesthetic being used. 20 c.cs of Perabrodil 35% were injected into the femoral artery, and films were taken of the thigh and leg. A doubtful break in the continuity of the popliteal artery was suggested, though this was not confirmed at subsequent operation. However, rapid filling of the popliteal and femoral veins was noted, a point recognised to be distinctive of arterio-venous fistulae. The anterior tibial and peroneal arteries were visualised normally.

Blood Volume.

As estimated by the Evans Blue method, the following figures were obtained:-

Blood volume = 4650 c.c.
= 88.1 c.c. per Kg.
= 3090 c.c. per sq. metre.

The blood volume was slightly high but no comparable figures for a child were available.

DIAGNOSIS.

A confident diagnosis of arterio-venous fistulae was made. Arteriography suggested an abnormality in relation to the popliteal vessels, but, as the hypertrophy involved the entire lower limb and buttock, it was probable that the iliac vessels were likewise affected.

TREATMENT.

Operation.

Under /

Under a general anaesthetic, operation was carried out by Professor J.R. Learmonth and myself. The incision of Fiolle was used to expose the lower part of the femoral artery and the popliteal artery. From the upper half of the popliteal artery arose six small abnormal branches, which ran anteriorly and became incorporated in a large venous plexus lying in close apposition to the posterior surface of the femur, that is, at the site of the angioma of the femur. These arteries were ligated and divided. Fairly brisk haemorrhage took place from the venous plexus and it was not thought advisable to investigate more fully the communications between the arteries and the plexus and between the plexus and the interior of the bone. It was felt that these anomalous arteries were definitely carrying blood directly into the veins and into the bony lesion.

Injection Treatment.

Injections of lithium salicylate were given after three weeks with a view to sclerosing the large prominent veins on the lateral side of the limb. A moderate degree of thrombosis was obtained though further injections would be required.

X-Ray Therapy.

This was started three weeks after operation, and was administered over a period of 17 days. The angioma of the lower end of the femur was irradiated, a dose of 4000r being given. The purpose of the treatment was, primarily, to effect the irradiation of the angioma, and secondarily, to reduce the growth in length at the lower end of the femur by irradiation of the epiphyseal cartilage.

SUBSEQUENT COURSE.

Eight months after operation, the patient was re-examined. The general appearances remained as before and he did not have any complaints. There was a slight increase in the boy's size, but without any outstanding difference in the affected limb. X-Ray examination showed no change.

COMMENT.

This case was an excellent example of arteriovenous fistulae, as proved by more recent methods of investigation. On purely clinical examination, many names might be applied, such as haemangiectatic hypertrophy, diffuse phlebectasis, various types of angioma, Klippel and Trenaunay syndrome, Parkes Weber syndrome, syndrome of varicose veins, angiomata and osteohypertrophy. Such diagnoses have been made frequently in the/

the past, yet it is certain that many of these cases were actually examples of arterio-venous fistulae.

In this case, the most prominent clinical features were the large size of the one lower limb, the angiomata, the anomalous varicose vein, the increased temperature of the limb, the increase in pulse rate on standing, and the increased blood pressure in the limb, all of which might well have been produced by a state of phlebectasia or by arterio-venous fistulae. The absence of abnormal pulsations in arteries and especially veins, and the absence of a bruit or a thrill in the veins did not prohibit a diagnosis of arterio-venous fistulae. The estimation of the oxygen content of the venous blood was without doubt the most significant single test, as a high reading gave quite conclusive evidence of the presence of abnormal arterio-venous communications. The fractional method of collecting specimens, described by Veal and McCord (57) was not carried out but, by its use, a possible site of the fistulae might have been suggested. For this latter purpose, however, arteriography, more accurate but more difficult technically, was carried out, and though it showed no actual fistulae, there was rapid abnormal filling of the popliteal and femoral veins. This finding, in conjunction with the abnormal structure of the lower end of the femur, suggested the advisability of the operation of exploration of the femoral and popliteal vessels.

The abnormal appearance of the lower end of the femur on X-Ray examination was of great interest and very rare. Examination of the X-Ray films alone might have suggested the more common possibilities such as giant cell tumour, osteitis fibrosa cystica, or sarcoma, and the absence of phleboliths in the soft parts did not indicate an obvious vascular lesion. Co-ordination of the X-Ray findings and the other observations made the diagnosis of angioma of the femur highly probable, though there are recorded cases of angioma of bone without other changes. A full discussion of this bony condition is given later. It is to be noted, however, that though some authorities believe angioma of bone to be a true tumour, others believe it to be a vascular malformation. Certainly findings at operation in this case were in favour of the latter. Good references to this subject are given by Bucy (135) and Bucy and Capp (136). Among previously quoted cases are those by Reid (1925)(72), case 31 of his series, and Duncan (1900)(10), case 2.

The operation revealed no obvious large arterio-venous communication, which result was anticipated by the absence of any abnormal pulsation, thrill or bruit. The six abnormal branches of the popliteal artery denoted an error in development and in their appearance they resembled those found at operation in well /

well-known recorded cases such as those of Reid (1925) (72) case 30, and Rienhoff (1924)(22). Owing to haemorrhage, it was not possible to trace them to their ultimate termination, but they either ran directly into the bone or into the venous plexus on the posterior aspect of the femur. As these abnormal arteries and veins had intimate relationship with the bone, it was reasonable to assume that they actually communicated with the interior of it, that is with the angioma. Biopsy of the bone was not attempted as severe haemorrhage could have been anticipated with certainty. The arteries were divided and ligated without difficulty and the operation terminated. One felt that the abnormal blood supply to the angioma of the femur had been greatly reduced but it was impossible to decide on the presence or absence of further vascular abnormalities elsewhere in the limb. Estimation of the oxygen content of the venous blood after operation revealed a greater degree of success than was believed, as the previous high reading was now replaced by a normal reading. This result, therefore, showed that several patent abnormal arterio-venous communications had been obliterated.

As the hypertrophy affected the buttock and the entire limb, it seemed highly probable that arterio-venous fistulae also involved either the common iliac vessels or else both the internal and external iliac vessels on that side. The inaccessible site and the vascularity would make any operation on them most hazardous, which was therefore not contemplated.

The results of the X-Ray treatment could not be estimated at once and repeated examinations would require to be carried out. The aims of the treatment were to irradiate the angioma with a view to its cure and to irradiate the adjacent epiphyseal cartilage in order to cause a slowing of the rate of growth at that part.

The ultimate prognosis must be guarded, though in all probability it will be satisfactory. For years after an apparently successful operation, there may be quiescence of the lesion and an adequate circulation to the distal part of the limb. Thereafter, there is liable to develop a state where new arterio-venous fistulae may open up, the vascular malformation may extend and a state of inadequate circulation may develop, with ulceration and gangrene. Such results have been described by several authors, for example, Pemberton and Saint (35), Dickson Wright (70). Then, also, there is the risk of cardiac failure developing as the consequence of the fistulae. The inequality of the limbs is liable to give rise to a progressive disability and, in particular, chronic arthritis of the sacro-iliac joints /

joints and scoliosis may be serious. The results of the treatment already carried out will be awaited with interest during the next few years.

As regards further steps in treatment, it might become necessary to repeat X-Ray treatment, for the same reasons as before. Also this treatment could be applied to one or more additional epiphyseal cartilages in the limb, should excessive growth continue. Alternatively, a form of leg equalisation operation might be considered, once growth had ceased.

There are many references to cases allied to this one in nature, apart from the problem of angioma of bone. The most recent and valuable are probably those of Reid (72), Pemberton and Saint (35), Dean Lewis (41), De Takats (51), Horton and Ghormley (94), Veal and McCord (57) and Homans (86).

To summarise, a report has been given of a case of arterio-venous fistulae of the popliteal and iliac vessels.

Figs. 12 & 13, Case 3. Large size of left lower limb with increase in girth and in length, producing tilting of pelvis; widespread haemangiomata; large varicose vein on lateral side.

Figs. 14 & 15, Case 3. X-Ray films - angioma of lower end of diaphysis of femur.

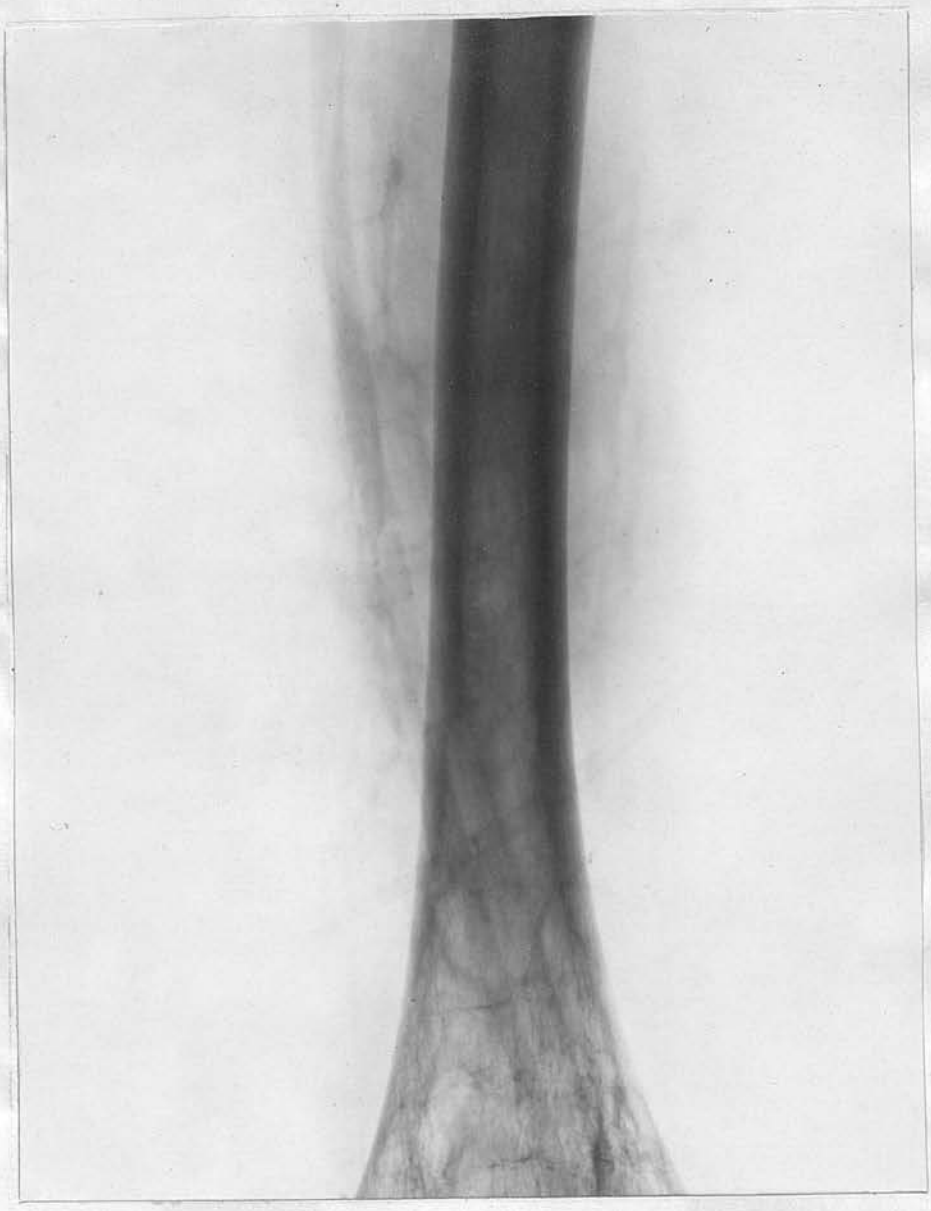


Fig. 16, Case 3. Arteriogram - visualisation of femoral and popliteal artery and vein, with rapid filling of latter.

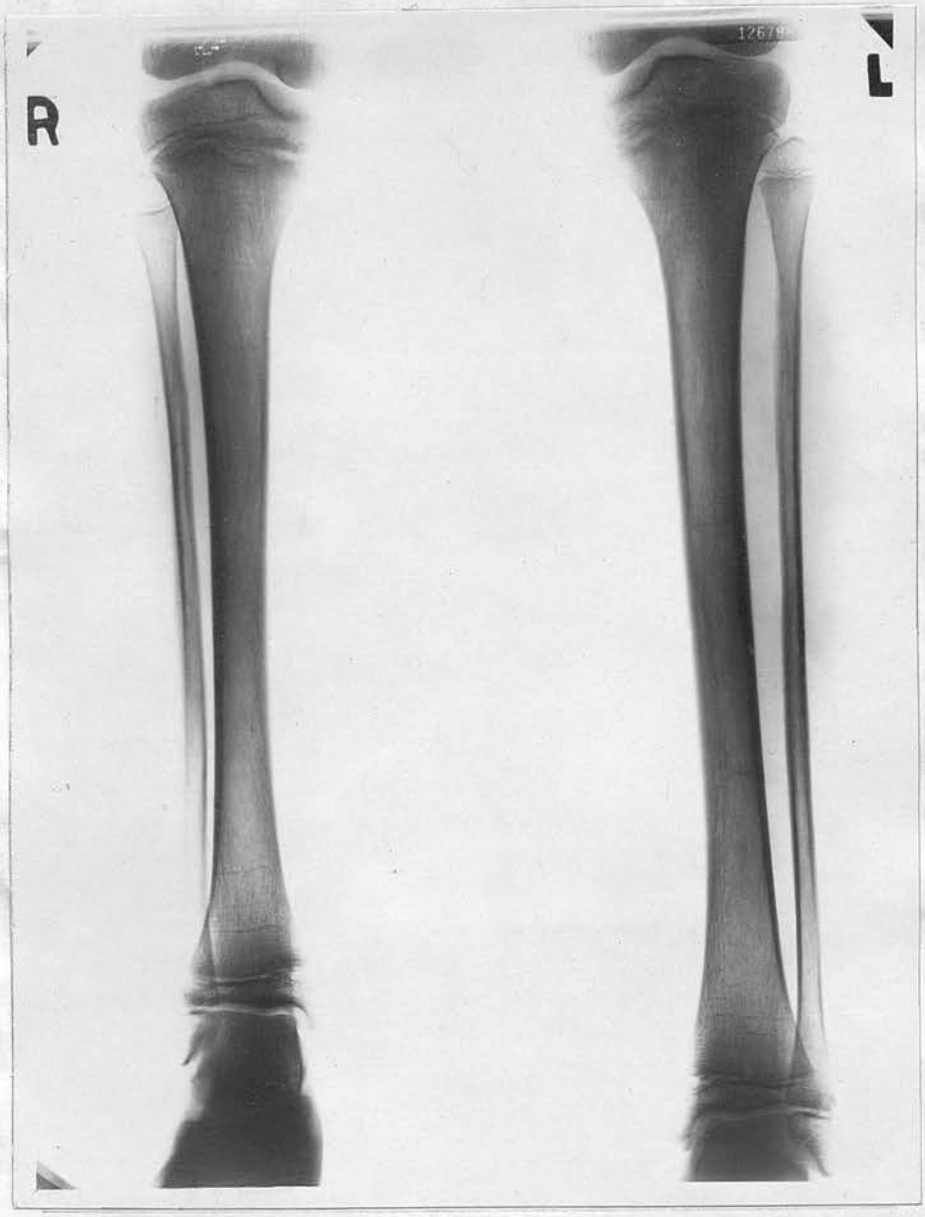


Fig. 17, Case 3. X-Ray film of both legs - increase in size of left tibia and fibula, but no structural change.

CASE 4.

T. H. Male Aged 8.

HISTORY.

This boy was born with the left lower limb larger than the right. The inequality of the limbs had caused no disability until recently, when pain in the left inguinal region came on after exercise. He was strongly built and quite normal in all other respects. There was no family history of similar deformity.

CLINICAL FEATURES.

Angiomata.

These were not pronounced. There was one large superficial capillary haemangioma, of faint pink colour, which involved the skin of the region of the greater trochanter and the buttock of the left side. It stretched for about an inch to the right of the mid line posteriorly. A small capillary haemangioma, about 1 inch in diameter, was present on the medial side of the left hand.

Hypertrophy of the Left Lower Limb.

There was a gross increase in size of the entire left lower limb, involving both length and circumference, and quite uniform in character. The changes were less marked in the toes. Tilting of the pelvis and scoliosis were naturally produced on standing erect, and the position of comfort assumed then was usually with the hip and knee slightly flexed. The movements and function of the limb were quite normal but its circumference increased considerably on standing. The opposite lower limb, the upper limbs and the trunk were of normal size. The following were the more important measurements:-

Length. Anterior superior iliac spine - medial malleolus.

R. 28 ins. L. 30 ins.

Anterior superior iliac spine - adductor tubercle.

R. 13¼ ins. L. 14 ins.

Foot R. 8 ins. L. 8¼ ins.

Circumference /

Circumference	Right.	Left - limb elevated.	Left - limb dependent.
Mid thigh	14½ ins.	16 ins.	17 ins.
Knee	11 ins.	13 ins.	14 ins.
Mid-calf	10 ins.	13 ins.	13½ins.
Ankle	6¾ ins.	8 ins.	8½ins.
Foot-instep	8 ins.	9 ins.	9½ins.

Varicose Veins.

Moderately dilated tortuous superficial veins were present around the left greater trochanter and on the anterior surface of the thigh. The long saphenous vein was visibly and palpably enlarged but was straight. There were no other obvious varicosities.

Local Circulatory Effects.

Definite abnormal pulsations were present in the veins in the region of the left groin and thigh. A forcible systolic thrill and a soft blowing systolic bruit were present over the external iliac artery and upper 2 inches of femoral artery with maximum intensity about 1 inch superior to inguinal ligament. The state of the circulation in the limb was satisfactory and there was no evidence of ulceration, particular attention being given to the toes. As already noted, there was marked enlargement of the limb on standing, so that all veins became tense and the circumference of the limb became increased. The entire limb was warmer to touch than the rest of the body.

General Cardio-Vascular Effects.

Interesting changes were present in the pulse rate. With the patient lying, it was 72 per minute, whereas on standing, it rose to 88. This observation in all probability indicated that a considerable quantity of circulatory blood passed into large venous spaces in the lower limb and thus became lost from the general circulation. On exerting firm pressure over the upper end of the femoral artery, the pulse rate fell to 64 per minute, thus illustrating the presence of the well known Branham or Nicoladoni bradycardia re-action. Examination had already suggested that one or more arterio-venous fistulae involved the iliac vessels, but the positive bradycardia re-action indicated conclusively that other fistulae existed in the femoral vessels or beyond. Blood pressure /

pressure variations were present. The general blood pressure, as measured in the arms and right thigh, was 122/82, whereas in the left lower limb it was 152/92. This variation in blood pressure is a well recognised feature of such cases, but it is generally believed to be variable in its occurrence and in its importance.

SPECIAL EXAMINATIONS.

Skin Temperature Tests.

Using the standard electric galvanometer, and at an average room temperature of 19.5°C, temperature readings were recorded at different levels on the anterior aspects of both lower limbs. They showed a very marked rise of temperature of the whole of the left lower limb, which confirmed the clinical observations:-

	Right.	Left.
Mid thigh	31°C	35°C
Knee	30	32.5
Middle of tibia	27	29
Ankle	25.5	30
Middle of foot	25.5	30
Great toe	22	23.5

Oxygen Content of Venous Blood.

Estimations were made of oxygen content of blood withdrawn from several veins. These tests were very instructive, showing how samples obtained at different levels of the affected limb may vary greatly. The important results were obtained from superficial veins at the following levels:- left elbow 15.3 volumes %; left knee (from long saphenous vein) 15.5 volumes %; left thigh (from superficial vein near groin) 22.7 volumes %. If the last sample had not been collected, a serious error would then have been made. The test confirmed the results of Veal and McCord (57) regarding the collection of blood at different levels.

Straight X-Ray Examination.

No abnormality of the bony structure of the left lower limb was present. Taken on the same film, the marked difference in size of the two legs was apparent.

Arteriography/

Arteriography.

Arteriography was not carried out. With the probable fistulous communications in the pelvis, it would have been technically difficult and dangerous to carry out the test.

DIAGNOSIS.

The certain diagnosis of arterio-venous fistulae could be made, on account of the pulsations in the veins, the palpable thrill, the audible bruit, and the high oxygen content of the venous blood. In all probability, one or more fistulae were in relation to the iliac vessels and one or more in relation to the upper end of the femoral vessels.

TREATMENT.

No operative treatment was carried out. Any attempt to expose the iliac vessels and to ligate fistulous communications would have been a difficult and perhaps hazardous undertaking and ligation of the common or external iliac artery alone would have been of no benefit. To counteract the inequality of the limbs, the smaller, normal limb was fitted with a high boot, which proved quite satisfactory and allowed the boy to walk with greater comfort. Two injections of lithium salicylate were given into the long saphenous vein in the thigh, causing a short lived localised thrombosis.

COMMENT.

This case was a good example of the classical type of arterio-venous fistulae. In the general appearances, there was a close resemblance to the previous case, with the hypertrophy of the limb, the angiomata, the dilated veins and the increased temperature, and again it was to be noted how these features have been described in both phlebectasis and arterio-venous fistulae. The other, more positive, signs of the latter were the strong thrill, the loud bruit, and the pulsation of the veins in the thigh.

Having determined the presence of the fistulae by these observations, it was then necessary to try to localise the site. The fact that the entire gluteal region was hypertrophied, as well as the rest of the limb, showed that the fistulae probably involved the common iliac vessels or else both the external and the internal iliac vessels. The bruit was maximal in intensity over the external iliac vessels one /

one inch proximal to the inguinal ligament, suggesting one or more fistulae at about that level. The positive Nicoladoni test was also important as pressure over the femoral artery produced a reflex fall in pulse rate from 72 to 64 per minute. This effect would only have been produced if fistulae had existed distal to the point of pressure. All these signs, therefore, indicated the widespread and multiple nature of the abnormality affecting the iliac and femoral vessels. The presence of the thrill, the bruit and the abnormal pulsation in the veins showed that the fistulae were large, and that more arterial blood passed through them than in the previous case.

The importance of the oxygen estimation of the venous blood was well emphasised. The fractional method of collecting the specimens, as recommended by Veal and McCord (57), showed how blood obtained from a superficial vein in the upper part of the thigh gave a much higher reading than that from the long saphenous vein at the level of the knee. According to these authors, this result indicated the presence of arterio-venous fistulae at the proximal part of the limb, but not as far distally as the knee. The failure to carry out the test might well have been the cause of difficulty in diagnosis.

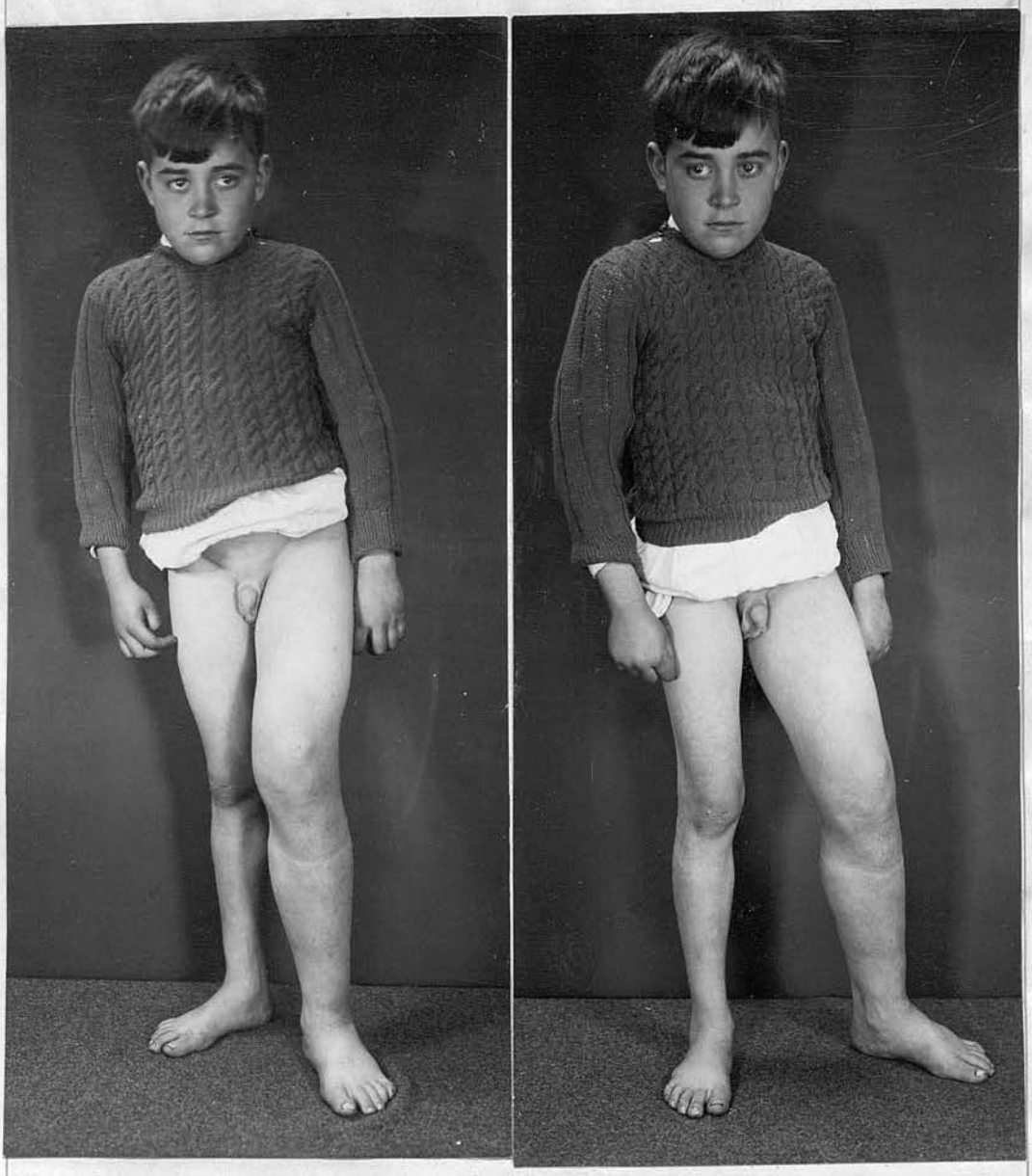
Little treatment was carried out, except the injections of a sclerosing solution into the varicose veins and the fitting of a high boot. The multiplicity of the fistulae and the great difficulty in closing them made a radical operation scarcely justifiable and there were neither severe local nor systemic effects to demand any immediate operation. Horton, quoted by Franklin (124), believed that an operation in such a case might make the condition worse, and he recommended orthopaedic correction of the affected limb, with amputation perhaps necessary in a severe case with systemic effects. The ultimate aim in treatment is, therefore, on similar lines and directed towards the deleterious effects of having one lower limb two inches longer than the other. In addition to the obvious inconvenience, there is a considerable risk of permanent scoliosis and chronic sacro-iliac arthritis developing later, an example of the latter being reported by Thomson (1932)(43). The operative methods of overcoming the deformity are applicable after growth has ceased and consist of increasing the length of the smaller limb or shortening the length of the larger limb. Another method is to apply X-Ray treatment at once to the epiphyseal cartilages of the affected limb, with a view to restricting further growth. A discussion on these methods will be given in a later section.

The ultimate prognosis is uncertain, but at the /

the moment, it seems satisfactory. There are, however, the risks of further fistulae becoming patent and of interference with satisfactory circulation in the distal part of the limb. There is also a grave risk of cardiac failure developing after many years, which is suggested by the presence of fistulae large enough to produce the cardio-vascular signs already mentioned. Amputation must also be constantly kept in mind, either because of severe local effects or because of severe cardiac failure.

The references to the literature given in the report on Case 3 are suitable for this case also. It is interesting to note that Hewett (1867)(4) recorded a case similar to the present one in which an arterio-venous fistula existed between the common iliac artery and vein; the final result was not stated.

To summarise, a report has been given of a case of multiple arterio-venous fistulae of the iliac and femoral vessels.



Figs. 18 & 19, Case 4. Large size of left lower limb, with increase in girth and in length producing tilting of pelvis; faint discolouration of leg due to haemangiomata; varicose vein visible in region of ankle.

Fig. 20, Case 4. As in previous illustrations.

Fig. 21, Case 4. X-Ray film of both legs - increase in size of left tibia and fibula but no structural change.

CASE 5.

E. A. Male Aged 13.

HISTORY.

This boy attended the Royal Infirmary, Edinburgh, for the first time in May 1935. Since birth, the second toe of the left foot had been enlarged and of greater size than the great toe. Three years previously, the skin on the medial side of the second toe broke down, resulting in ulceration and slight haemorrhage. Only temporary healing took place. Four weeks before admission, the foot became greatly swollen. There was no family history of a similar deformity.

CLINICAL FEATURES.

The whole of the left foot was swollen, especially the distal half, and it was soft on palpation. The second toe was large, with ulcers on the medial and lateral sides. In the space between the first and second metatarsals, on the dorsal surface, there were present marked pulsations, a palpable thrill and a loud, rough bruit, audible with each systole. The pulse rate with the patient resting was 72 per minute, and on compression of the anterior tibial artery, it was 66 per minute.

SPECIAL EXAMINATIONS.

Straight X-Ray Examination.

This showed generalised rarefaction of the distal part of the foot, most noticeable in the head of the second metatarsal and in the second toe. In addition, the base of the first phalanx of the second toe showed a well marked cystic change. The increased length of the second, and, to a less degree, the third toes was evident.

Arteriography.

The anterior tibial artery was exposed above the laciniate ligament and was found to be enlarged and the size of a normal brachial artery. A tourniquet was applied, 2.5 c.c of thorotrast were injected, and the first exposure to X-Rays made. After another injection of 2.5 c.c of thorotrast, a second exposure was made. A final injection of saline followed. The enlarged anterior tibial and dorsalis pedis arteries, and /

and the first dorsal and first plantar interosseous arteries were well shown. At the distal end of the first interosseous space, there was the elongated saccular dilatation of a venous lacuna. Several small branches were noted in the vicinity of the second metatarso-phalangeal joint.

As this examination was not completely satisfactory, arteriography was repeated, this time thorotrast being injected into the femoral artery. The resulting film showed a plexus of greatly dilated vessels, including particularly the dorsalis pedis, medial plantar and lateral plantar arteries and numerous very tortuous veins. This abnormality was most intense around the metatarso-phalangeal joints of the second toe, and to a less degree around the third toe, and on account of the numerous vessels, it was not easy to trace the course of any single one. It seemed, however, as though all the dilated vessels in the foot converged on or diverged from this point. The result of these investigations was that several small arterio-venous fistulae were demonstrated in the region of the base of the second toe, probably both in the soft tissues and in the bones. Another, most significant feature was that the distal parts of the second and third toes and all of the other toes showed a very poor blood supply, in spite of the great amount of blood passing into the foot.

TREATMENT.

Operation.

Two months after admission, Mr. W.A. Cochrane operated, using a tourniquet. A longitudinal incision was made on the dorsum of the foot over the enlarged vessels. These were dissected out and several enlarged arterial and venous trunks found in the first interosseous space were ligated and divided. Another longitudinal incision was made on the medial side of the foot, over the medial plantar vessels, which were also ligated and divided. The operation, therefore, consisted of proximal ligation of the abnormal dorsalis pedis and medial plantar vessels. A good recovery took place with loss of the thrill and the bruit, but the sore on the second toe remained.

SUBSEQUENT COURSE.

The patient was re-admitted to hospital three years later, i.e. in 1938. There had been a short period of improvement after the operation, but the condition had then gradually deteriorated, until it had become quite acute in the last eight months, so that pain /

and the first dorsal and first plantar interosseous arteries were well shown. At the distal end of the first interosseous space, there was the elongated saccular dilatation of a venous lacuna. Several small branches were noted in the vicinity of the second metatarso-phalangeal joint.

As this examination was not completely satisfactory, arteriography was repeated, this time thorotrast being injected into the femoral artery. The resulting film showed a plexus of greatly dilated vessels, including particularly the dorsalis pedis, medial plantar and lateral plantar arteries and numerous very tortuous veins. This abnormality was most intense around the metatarso-phalangeal joints of the second toe, and to a less degree around the third toe, and on account of the numerous vessels, it was not easy to trace the course of any single one. It seemed, however, as though all the dilated vessels in the foot converged on or diverged from this point. The result of these investigations was that several small arterio-venous fistulae were demonstrated in the region of the base of the second toe, probably both in the soft tissues and in the bones. Another, most significant feature was that the distal parts of the second and third toes and all of the other toes showed a very poor blood supply, in spite of the great amount of blood passing into the foot.

TREATMENT.

Operation.

Two months after admission, Mr. W.A. Cochrane operated, using a tourniquet. A longitudinal incision was made on the dorsum of the foot over the enlarged vessels. These were dissected out and several enlarged arterial and venous trunks found in the first interosseous space were ligated and divided. Another longitudinal incision was made on the medial side of the foot, over the medial plantar vessels, which were also ligated and divided. The operation, therefore, consisted of proximal ligation of the abnormal dorsalis pedis and medial plantar vessels. A good recovery took place with loss of the thrill and the bruit, but the sore on the second toe remained.

SUBSEQUENT COURSE.

The patient was re-admitted to hospital three years later, i.e. in 1938. There had been a short period of improvement after the operation, but the condition had then gradually deteriorated, until it had become quite acute in the last eight months, so that pain /

pain, throbbing and swelling in the foot were severe complaints. The foot was now swollen and deeply pigmented in irregular patches, and there were ulcers over the full length of both sides of the second toe. Pulsation in the veins, a palpable thrill and a loud bruit were present, most noticeable in the middle of the dorsum of the foot. Gangrene of the foot was imminent, and it was obvious that the part could not be saved. Accordingly, Mr. W. A. Cochrane carried out an amputation of the leg, seven inches below the knee, using a long anterior flap. The amputated part was not preserved for further inspection. The wound in the leg healed without difficulty and an artificial limb was fitted five months later.

PERSONAL EXAMINATION.

I saw the patient for the first time in 1942. He walked very well with the artificial limb, without any limp. The result of the amputation was excellent, as the stump was quite painless and not swollen, and without any sign of the recurrence of the arterio-venous fistulae. A search was made for further abnormalities in other parts of the body, but the only one was a small, superficial, capillary haemangioma, $\frac{1}{2}$ inch in diameter, situated over the greater trochanter of the opposite thigh, and quite symptomless.

An unfortunate complication of a different nature was present. The patient had been in poor general health for several months, suffering from abdominal pain, shortness of breath, cough and anaemia. Clinical and X-Ray examination revealed the presence of tuberculosis at the apices of both lungs. The pulse rate, even while resting, was 100 per minute, and the heart was enlarged, with the apex beat four inches from the mid line in the sixth left intercostal space. The patient was referred to the local Tuberculosis Authorities for admission to a sanitorium.

COMMENT.

This case was a classical example of arterio-venous fistulae but differed from case 4 in that the distal part of the limb was primarily involved, not the proximal. It was a well recognised type of lesion, often known as a cirsoid aneurysm, though in the past many varying names might have been applied, such as aneurysm by anastomosis, plexiform angioma, pulsating angioma or naevus, phlebarteriectasis, angioma of bone, or angiosarcoma.

There was no doubt about the congenital origin, though serious effects did not arise until the age/

age of thirteen, after which they became progressive. The paradoxical results of this type of lesion were well illustrated, as, in spite of the tremendous increase of vascularity of the foot, there were signs of insufficiency of the digital circulation, so that there was persistent ulceration of the second toe. The presence of abnormal arterio-venous communications was well shown by the marked pulsation in the veins of the foot, the palpable thrill, the loud bruit and the positive Branham or Nicoladoni bradycardia test. The degree of osteohypertrophy was slight compared to the other cases in this series and showed itself only in an increase in size of the second and third toes. Unlike many other cases, there were no angiomata in the skin of the affected part, though a small capillary angioma was situated in the region of the greater trochanter of the healthy limb. The pigmentation of the foot which appeared in the later stages, was probably due to the deposition of blood pigment and not due to an angioma.

X-Ray examination of the foot showed marked rarefaction of the bones, presumably due to hyperemic decalcification. It also revealed an uncommon cyst-like change in the first phalanx of the second toe. This was intimately related to the vascular abnormality of the soft parts, and it was over this area that the abnormal pulsations, the thrill and the bruit were maximum. This lesion was presumed to be an angioma of the bone, meaning a vascular abnormality, not an actual tumour; and it seemed highly probable that it contained many vascular channels through which arterial blood circulated.

Arteriography, with the injection of thorotrast into the femoral artery, gave a good impression of the tremendous vascularity of the foot, with many large communicating vessels forming a dense plexus. It showed how the region of the base of the first phalanx of the second toe seemed to be the centre of the abnormality and how several fistulae appeared to exist there, though it was not easy to trace out any single channel. Another important point, confirming the clinical impressions, was the very poor blood supply to the digits, showing that the arterial blood travelled directly into the veins and by-passed the digital circulation. The investigation must surely have been one of the earliest arteriographies to be carried out for congenital arterio-venous fistulae of the limbs. Horton and Ghormley (95) claimed that, in the same year, 1935, they were the first to carry out such an investigation.

The operation performed in 1935 was necessarily in the nature of a proximal ligation of the enlarged, tortuous dorsalis pedis and medial plantar arteries, with /

with ligation of their accompanying veins. Any direct approach to the fistulae at the base of the second toe would scarcely have been attainable. The immediate result was a loss of the abnormal pulsations, the thrill and the bruit, but a persistence of the ulceration of the toe. Possibly a small amount of arterial blood still passed directly into the veins.

Three years later, in 1938, the condition of the foot was as bad as before the operation. After a brief period of improvement, there had thus occurred the usual sequelae of proximal ligation, namely, the recurrence of the original signs and the appearance of impending gangrene. Almost certainly new fistulae had become patent and an extensive collateral circulation had developed. There was thus a similarity to traumatic arterio-venous fistulae, and Reid (74) showed that either a traumatic or a congenital fistula was a powerful stimulus to the formation of a collateral circulation. As the foot was a hindrance to the patient and painful, amputation was the only treatment to be considered.

On examination in 1942, the amputation stump was excellent, and there was no evidence of a recurrence of the vascular lesion in the stump. Unfortunately, the patient was now suffering from pulmonary tuberculosis, and the dilated heart, the rapid pulse rate and the dyspnoea were no doubt the result of this, rather than an effect of the arterio-venous fistulae. The ultimate prognosis was thus difficult to assess, and was probably concerned chiefly with the progress of the tuberculosis.

There were several interesting references in the literature to cases of a similar nature in the hand or foot, the following being among the most important:- Bland Sutton (1918)(17); Armour (1919)(18); Bernheim (1925)(25); Dean Lewis (1930)(41); Veal and McCord (1936)(57); Horton and Ghormley (1935)(95); Holman (1937)(61); Reid and McGuire (1938)(77). Two cases, almost identical to the one being discussed, were reported by Gilmour and Bolam (1937-8)(60), the most prominent features being ulceration of the second toe, a dense network of vessels on arteriography, multiple fistulae and eventual amputation. Pemberton and Saint (1928)(35) gave an excellent account of similar lesions. Case 3 of their series, also reported by Matas (1940(36a), was an outstanding example of how the signs of arterio-venous fistulae can develop in the stump of a limb, after apparently successful amputation. The possibility of such a recurrence was borne in mind while examining my own case, though actually the amputation stump was perfectly healthy.

To summarise, a report has been given of a case of multiple arterio-venous fistulae of the foot.

and the first dorsal and first plantar interosseous arteries were well shown. At the distal end of the first interosseous space, there was the elongated saccular dilatation of a venous lacuna. Several small branches were noted in the vicinity of the second metatarso-phalangeal joint.

As this examination was not completely satisfactory, arteriography was repeated, this time thorotrast being injected into the femoral artery. The resulting film showed a plexus of greatly dilated vessels, including particularly the dorsalis pedis, medial plantar and lateral plantar arteries and numerous very tortuous veins. This abnormality was most intense around the metatarso-phalangeal joints of the second toe, and to a less degree around the third toe, and on account of the numerous vessels, it was not easy to trace the course of any single one. It seemed, however, as though all the dilated vessels in the foot converged on or diverged from this point. The result of these investigations was that several small arterio-venous fistulae were demonstrated in the region of the base of the second toe, probably both in the soft tissues and in the bones. Another, most significant feature was that the distal parts of the second and third toes and all of the other toes showed a very poor blood supply, in spite of the great amount of blood passing into the foot.

TREATMENT.

Operation.

Two months after admission, Mr. W.A. Cochrane operated, using a tourniquet. A longitudinal incision was made on the dorsum of the foot over the enlarged vessels. These were dissected out and several enlarged arterial and venous trunks found in the first interosseous space were ligated and divided. Another longitudinal incision was made on the medial side of the foot, over the medial plantar vessels, which were also ligated and divided. The operation, therefore, consisted of proximal ligation of the abnormal dorsalis pedis and medial plantar vessels. A good recovery took place with loss of the thrill and the bruit, but the sore on the second toe remained.

SUBSEQUENT COURSE.

The patient was re-admitted to hospital three years later, i.e. in 1938. There had been a short period of improvement after the operation, but the condition had then gradually deteriorated, until it had become quite acute in the last eight months, so that pain /

pain, throbbing and swelling in the foot were severe complaints. The foot was now swollen and deeply pigmented in irregular patches, and there were ulcers over the full length of both sides of the second toe. Pulsation in the veins, a palpable thrill and a loud bruit were present, most noticeable in the middle of the dorsum of the foot. Gangrene of the foot was imminent, and it was obvious that the part could not be saved. Accordingly, Mr. W. A. Cochrane carried out an amputation of the leg, seven inches below the knee, using a long anterior flap. The amputated part was not preserved for further inspection. The wound in the leg healed without difficulty and an artificial limb was fitted five months later.

PERSONAL EXAMINATION.

I saw the patient for the first time in 1942. He walked very well with the artificial limb, without any limp. The result of the amputation was excellent, as the stump was quite painless and not swollen, and without any sign of the recurrence of the arterio-venous fistulae. A search was made for further abnormalities in other parts of the body, but the only one was a small, superficial, capillary haemangioma, ½ inch in diameter, situated over the greater trochanter of the opposite thigh, and quite symptomless.

An unfortunate complication of a different nature was present. The patient had been in poor general health for several months, suffering from abdominal pain, shortness of breath, cough and anaemia. Clinical and X-Ray examination revealed the presence of tuberculosis at the apices of both lungs. The pulse rate, even while resting, was 100 per minute, and the heart was enlarged, with the apex beat four inches from the mid line in the sixth left intercostal space. The patient was referred to the local Tuberculosis Authorities for admission to a sanitorium.

COMMENT.

This case was a classical example of arterio-venous fistulae but differed from case 4 in that the distal part of the limb was primarily involved, not the proximal. It was a well recognised type of lesion, often known as a cirsoid aneurysm, though in the past many varying names might have been applied, such as aneurysm by anastomosis, plexiform angioma, pulsating angioma or naevus, phlebarteriectasis, angioma of bone, or angiosarcoma.

There was no doubt about the congenital origin, though serious effects did not arise until the age/

age of thirteen, after which they became progressive. The paradoxical results of this type of lesion were well illustrated, as, in spite of the tremendous increase of vascularity of the foot, there were signs of insufficiency of the digital circulation, so that there was persistent ulceration of the second toe. The presence of abnormal arterio-venous communications was well shown by the marked pulsation in the veins of the foot, the palpable thrill, the loud bruit and the positive Branham or Nicoladoni bradycardia test. The degree of osteohypertrophy was slight compared to the other cases in this series and showed itself only in an increase in size of the second and third toes. Unlike many other cases, there were no angiomata in the skin of the affected part, though a small capillary angioma was situated in the region of the greater trochanter of the healthy limb. The pigmentation of the foot which appeared in the later stages, was probably due to the deposition of blood pigment and not due to an angioma.

X-Ray examination of the foot showed marked rarefaction of the bones, presumably due to hyperemic decalcification. It also revealed an uncommon cyst-like change in the first phalanx of the second toe. This was intimately related to the vascular abnormality of the soft parts, and it was over this area that the abnormal pulsations, the thrill and the bruit were maximum. This lesion was presumed to be an angioma of the bone, meaning a vascular abnormality, not an actual tumour; and it seemed highly probable that it contained many vascular channels through which arterial blood circulated.

Arteriography, with the injection of thorotrast into the femoral artery, gave a good impression of the tremendous vascularity of the foot, with many large communicating vessels forming a dense plexus. It showed how the region of the base of the first phalanx of the second toe seemed to be the centre of the abnormality and how several fistulae appeared to exist there, though it was not easy to trace out any single channel. Another important point, confirming the clinical impressions, was the very poor blood supply to the digits, showing that the arterial blood travelled directly into the veins and by-passed the digital circulation. The investigation must surely have been one of the earliest arteriographies to be carried out for congenital arterio-venous fistulae of the limbs. Horton and Ghormley (95) claimed that, in the same year, 1935, they were the first to carry out such an investigation.

The operation performed in 1935 was necessarily in the nature of a proximal ligation of the enlarged, tortuous dorsalis pedis and medial plantar arteries, with /

with ligation of their accompanying veins. Any direct approach to the fistulae at the base of the second toe would scarcely have been attainable. The immediate result was a loss of the abnormal pulsations, the thrill and the bruit, but a persistence of the ulceration of the toe. Possibly a small amount of arterial blood still passed directly into the veins.

Three years later, in 1938, the condition of the foot was as bad as before the operation. After a brief period of improvement, there had thus occurred the usual sequelae of proximal ligation, namely, the recurrence of the original signs and the appearance of impending gangrene. Almost certainly new fistulae had become patent and an extensive collateral circulation had developed. There was thus a similarity to traumatic arterio-venous fistulae, and Reid (74) showed that either a traumatic or a congenital fistula was a powerful stimulus to the formation of a collateral circulation. As the foot was a hindrance to the patient and painful, amputation was the only treatment to be considered.

On examination in 1942, the amputation stump was excellent, and there was no evidence of a recurrence of the vascular lesion in the stump. Unfortunately, the patient was now suffering from pulmonary tuberculosis, and the dilated heart, the rapid pulse rate and the dyspnoea were no doubt the result of this, rather than an effect of the arterio-venous fistulae. The ultimate prognosis was thus difficult to assess, and was probably concerned chiefly with the progress of the tuberculosis.

There were several interesting references in the literature to cases of a similar nature in the hand or foot, the following being among the most important:- Bland Sutton (1918)(17); Armour (1919)(18); Bernheim (1925)(25); Dean Lewis (1930)(41); Veal and McCord (1936)(57); Horton and Ghormley (1935)(95); Holman (1937)(61); Reid and McGuire (1938)(77). Two cases, almost identical to the one being discussed, were reported by Gilmour and Bolam (1937-8)(60), the most prominent features being ulceration of the second toe, a dense network of vessels on arteriography, multiple fistulae and eventual amputation. Pemberton and Saint (1928)(35) gave an excellent account of similar lesions. Case 3 of their series, also reported by Matas (1940(36a), was an outstanding example of how the signs of arterio-venous fistulae can develop in the stump of a limb, after apparently successful amputation. The possibility of such a recurrence was borne in mind while examining my own case, though actually the amputation stump was perfectly healthy.

To summarise, a report has been given of a case of multiple arterio-venous fistulae of the foot.

Figs. 22 & 23, Case 5. Ulceration of left second toe; greatly dilated vessels; cutaneous pigmentation.

Fig. 24, Case 5. X-Ray film - angioma of base of first phalanx of second toe, causing cyst-like appearance; osteoporosis of metatarsals and phalanges.

Fig. 25, Case 5. Arteriogram - great dilatation of dorsalis pedis artery and many veins; arterio-venous fistulae in region of base of second toe, with surrounding intense vascularity.

CASE 6.

W. C. Male Aged 55.

HISTORY.

At birth, a large haemangioma was present in the region of the mouth and the left side of the neck. It gradually became larger until it became the hugh unsightly mass which I saw for the first time in 1942. This increase in size was well borne out by comparison of photographs taken in the past and recently. There was no family history of a similar deformity. The general health was always good and the lesion was painless. Spontaneous haemorrhage did not take place, but severe bleeding of a spurting nature sometimes followed a small cut, as by a razor. Mastication was difficult and only soft or semi-solid foods were usually eaten. Difficulties with respiration and deglutition were only occasional features.

Treatment in the past had been carried out at different hospitals. During childhood, several operations had been attempted, only to be abandoned on account of haemorrhage. Thereafter, he was warned to avoid further operations as he "would surely bleed to death". On another occasion, treatment was given by electrolysis, but it was followed by severe oedema and great respiratory distress.

At the time of my examination, the patient was recovering from the effects of a severe circular saw injury of the right hand, which had produced considerable loss of function.

CLINICAL FEATURES.

The Haemangioma.

A most unsightly lesion, generally described as a cavernous haemangioma, involved the face, neck, lower lip, tongue and oral cavity. On the left side of the neck and face, it formed a very bulky, soft, compressible swelling, which stretched inferiorly to the cricoid cartilage, posteriorly to the sterno-mastoid muscle, and superiorly to the level of the tragus. Medially, a small extension of the lesion passed beyond the mid line of the neck to the right side. On the cutaneous surface of the swelling were many irregular, dilated veins, varying in size from $\frac{1}{4}$ inch in diameter to small telangiectatic spots. The skin had a generalised bluish discolouration. Several firm phleboliths were palpable.

The /

The lower lip was enormously hypertrophied and protuberant, so that it hung downwards towards the chin. The tongue was very large, could not be replaced within the mouth, and formed a hideous, permanent protrusion beyond the lower lip. Only a small range of movement was possible, and almost the whole of it was involved except for a small area on the dorsum. A continuous dribbling of saliva took place from the mouth. Both the lower lip and the tongue had irregular, nodular surfaces, and a dark purplish red colour, and were soft and compressible.

The floor of the mouth, the alveolar margins, and the mucosal surface of the left cheek were also extensively involved, and the lesion passed backwards and downwards into the pharynx as far as the eye could reach. The mucous membrane in these parts was again greatly hypertrophied and similar in appearance to the lower lip and tongue. A few small, bluish patches were present on the mucosal surface of the right cheek. Grossly carious teeth were present in both upper and lower jaws but they were almost completely buried in the hypertrophied mucous membrane. No dental extractions had ever been made but some had apparently fallen out spontaneously. The mandible could be easily palpated and gave the impression of being thin and atrophic.

The upper part of the face was normal and remarkably good looking with soft and gentle eyes. The patient was of a very pleasant disposition, in spite of the severe handicap of his disfigurement.

Phleboliths.

Several hard phleboliths were palpable in the subcutaneous tissues of the neck due to previous thrombosis in the veins. They were more prominent radiologically than clinically.

Local Circulatory Effects.

There was an absence of any thrill or bruit or pulsation in the veins of the affected part. There was no ulceration on the cutaneous or mucosal surfaces. As already mentioned, haemorrhage occasionally followed on injury but could always be stopped by firm pressure. No haemorrhage had ever taken place from around the teeth.

General Cardio Vascular Effects.

The pulse rate was 80 per minute and of normal rhythm. No bradycardia re-action could be elicited on pressure over the common carotid artery, proximal to the malformation. The blood pressure, as /

as measured in both brachial arteries, was 220/140. There was no evidence of arterio-sclerosis. The heart was enlarged, with the apex beat in the sixth left intercostal space, 4½ inches from the mid line. The heart sounds were closed, but the aortic second sound was accentuated. No symptoms were referable to the high blood pressure, and there was no evidence of cardiac failure. Urinary examination disclosed no pathological features.

SPECIAL EXAMINATIONS.

Oxygen Content of the Venous Blood.

A specimen of blood was withdrawn from one of the obvious superficial dilated veins of the neck, using the recognised technique. It was bright red in colour, and estimation showed an oxygen content of 18.2 volumes %. In comparison, blood withdrawn from a superficial vein in the right forearm was dark bluish red in colour and had an oxygen content of 9.7 volumes%.

X-Ray Examination.

In the neck, the obvious outline of the large soft tissue swelling was apparent. Scattered throughout the neck and oral region were a very large number of phleboliths, which gave a striking picture. They were quite opaque to X-Rays, varied in size and were round in shape. The mandible was atrophied and decalcified, but no other pathological change was present in it. The teeth showed considerable absorption of the roots and the crowns.

Arteriography was not attempted. The necessary exposure of the common carotid artery would have been hazardous and was not justifiable. It was not considered likely that venography would convey any new information.

DIAGNOSIS.

The general appearances suggested, and the high oxygen content of the venous blood made definite, a diagnosis of arterio-venous fistulae. These fistulae were believed to involve arteries derived from the external carotid artery and tributaries of the internal and external jugular veins. It was presumed that they were small and multiple, in view of the absence of abnormal pulsations, a thrill or a bruit.

TREATMENT /

TREATMENT.

Operative Treatment.

The patient was unwilling to submit to any operative treatment, in view of the lack of success in the past when the lesion was smaller. There was actually no indication for operation at his present age, as it was not producing dangerous effects, and was not much more disfiguring than it had ever been. Even if attempted, operation would have been very difficult and dangerous, without any certainty of a satisfactory result.

X-Ray Treatment.

It was thought possible that this might produce some diminution in the size of the lesion, though no hope of cure was entertained. Treatment was accordingly carried out by Dr. R. McWhirter in the Radiology Department, Royal Infirmary, Edinburgh. During March, April and May 1942, five treatments were given, with a total dosage of 1500 r. There was little re-action afterwards and in August 1942, a further dosage of 1000 r was administered. Following this, a deep slough developed in the lower lip, giving rise to ulceration and occasional bouts of severe bleeding. At the same time, other unpleasant effects were swelling of the tongue, difficulty in swallowing, slight respiratory distress and general discomfort, all of which passed off in a week. The ulcer on the lip slowly healed during the next two months.

SUBSEQUENT COURSE.

Little difference in the local condition could be detected after the treatment. Presumably the failure was due to the mechanical effect of the abnormal arterio-venous communications, which could not be expected to respond to radiotherapy any more than normal vessels.

The patient reported regularly until March 1943, but soon afterwards it was learned that he had committed suicide. He had been out of work as a result of the hand injury, and it seemed that the combination of this and the facial disfigurement had led him to take his life while in a mentally depressed state. It could not be determined if any intra-cranial vascular abnormality had existed.

COMMENT.

The patient was always believed to have suffered from an actual tumour, a cavernous haemangioma, and /

and certainly in such lesions this diagnosis has often been accepted. I propose to put forward the view that the essential underlying cause in this case was multiple arterio-venous fistulae due to a vascular malformation. The literature on the subject of these lesions is confusing and often contradictory, but a full review and a discussion will be given in a later section. Briefly, the supporters of the tumour theory believe that the haemangioma starts as a localised tumour, which may obtain connections with arteries and veins by a process of invasion, and that the main mass of the swelling is the result of proliferation of angioblastic tumour cells. Those who uphold the theory of a vascular malformation believe that one or more arterio-venous fistulae form the essential primary feature and that the main mass of the swelling is composed of veins which have become dilated through transmitting blood at an arterial pressure. Pathological examination often fails to be conclusive, showing merely many vessels and vascular spaces. My views are based on the results of the examination of this case and the comparison of it with other cases of mine and previously reported cases.

Clinical examination of the lesion showed that the swelling in the neck was composed chiefly of veins, which were in no way different from varicose veins seen in other conditions. The increase in size of the tongue and lower lip could no doubt be traced, in addition, to a general hypertrophy of all the soft tissues, as has been found so often in similar vascular lesions elsewhere. There was an absence of any abnormal pulsation, thrill or bruit, but this is known to be the case when the arterio-venous fistulae are small and multiple. There was also a complete absence of any capillary haemangioma. The most decisive test in arriving at a diagnosis was the estimation of the oxygen content of the venous blood, the specimen being withdrawn from a very superficial vein with no possibility of the needle having entered an artery inadvertently. The high reading of 18.2 volumes % showed that blood closely resembling arterial blood was flowing in the veins, and it was conclusive evidence of the presence of abnormal arterio-venous communications.

X-Ray examination showed a most outstanding picture. The phleboliths were widely scattered in the soft tissues and were very typical of this type of vascular lesion. The atrophy of the mandible, without any other pathological change in it, was most probably due to disuse, although it might have been the result of an abnormal blood supply. Arteriography would no doubt have shown the filling of the venous channels but the operative difficulties of exposing the common carotid artery did not justify it.

The /

The significance of the raised blood pressure and the hypertrophied heart was not certain. They might have been the result of long-standing arterio-venous fistulae, although cardio-vascular changes are much less common in congenital arterio-venous fistulae than in traumatic. On the other hand, a state of essential hypertension might have existed as an independent feature. The examination of the urine showed no abnormality and there was definitely an absence of the usual features of chronic nephritis with raised blood pressure.

In arriving at a diagnosis, it was necessary to decide whether the lesion was a true tumour, which had obtained a connection with the arteries, or whether it was a vascular malformation without any tumour formation. My conclusion, however, was that multiple arterio-venous fistulae existed between branches of the external carotid artery and tributaries of the internal and external jugular veins, due to a malformation of the developing vessels.

Treatment at the time I saw the patient first was obviously fraught with difficulties. It was hoped that X-Ray treatment might cause the swelling to shrink in size, but, in spite of heavy dosage, no improvement took place. This failure was believed to indicate that the swelling was composed of blood vessels of a normal structure and not of vascular spaces derived from immature tumour cells, in which case a response could have been anticipated. No operative treatment was considered, as the disfigurement was not much greater than ever before, nor was the lesion much more dangerous to life.

In enquiring into the treatment given in the past, it would appear that the operations were of an incomplete nature, in which severe haemorrhage was inevitable with no provision for its adequate control and with incisions made directly into the vascular area. Electrolysis was also carried out but gave rise to alarming results. The method was strongly advocated by Duncan (10), who reported considerable success in similar lesions.

It is instructive to consider what other methods of treatment might have been successful. At an earlier stage, perhaps, in childhood, before the lesion became so extensive, success might have followed a boldly planned operation. This would have entailed a wide exposure of the common carotid and external carotid arteries, thus allowing control of haemorrhage by temporary occlusion of them and permitting ligation and division of all branches of the latter artery passing into /

into the swelling. Excision of the main mass of dilated veins would have been feasible then and injections of a sclerosing solution into any remaining veins could have been carried out at the same time. An operation of such dimensions would, therefore, have given the patient a chance of a satisfactory cure. Alternatively, ligation of the external carotid artery might have been technically easier, to be followed by injection of the mass of veins.

There were several references in the literature to lesions of a like nature, involving the neck and mouth regions, and diagnosed variously as haemangiomata, cirsoid aneurysms and arterio-venous aneurysms. Among the early examples were those of Despres (1879) and Domainville (1883), both quoted by Rienhoff (22). Berry (1906)(12) described a large arterio-venous aneurysm of the neck and was one of the first investigators to suggest that the main mass of the swelling was composed of veins, not arteries nor tumour tissue. The result of his operation was brilliant and there is no reason to believe that a similar operation in the case under discussion would have been technically more difficult, if carried out at an earlier age.

There were other later accounts of similar lesions in which resourceful operations were followed by excellent results. The most important cases were those of Meleney (1923)(20); Rienhoff (1924)(22); Reid (1925)(72), case 30 of his series; Reid and McGuire (1938)(77), case 25 of their series; Ward and Horton (1940)(98), case 5 of their series. A different line of treatment was pursued by De Takats and McKenzie (1934)(52), case 9, in which obliterative injections alone gave a good result. This was a simple method and would have been attempted in my own case, if X-Ray treatment had not produced undesirable effects. Davies Colley (1940-41)(88) described three cases in the region of the face in only one of which was there complete relief following operation, and in another a fatal result ensued.

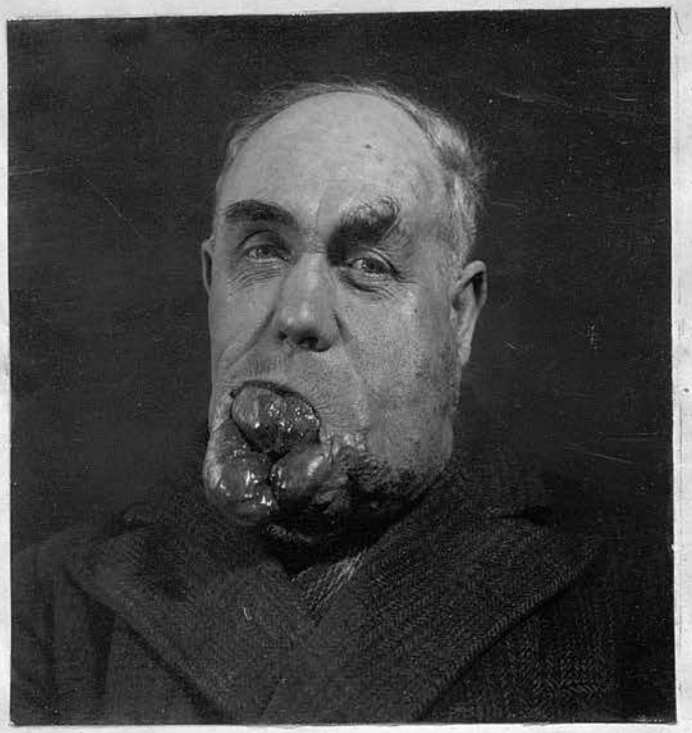
On the other hand, it is well to record the failures which may take place after an apparently successful operation. The well known case of **Halsted** (1919)(15), later reported by Reid (1925)(72), showed an initial period of success, but ultimately the condition deteriorated and further spread took place. Pemberton and Saint (1928)(35) also demonstrated failure in case 7 after a satisfactory operation. Schloffer (1930)(40) recorded a case of racemose arterial angioma, believed to be the result of arterio-venous fistulae, in which recurrence took place after operation and puncture with the galvano-cautery.

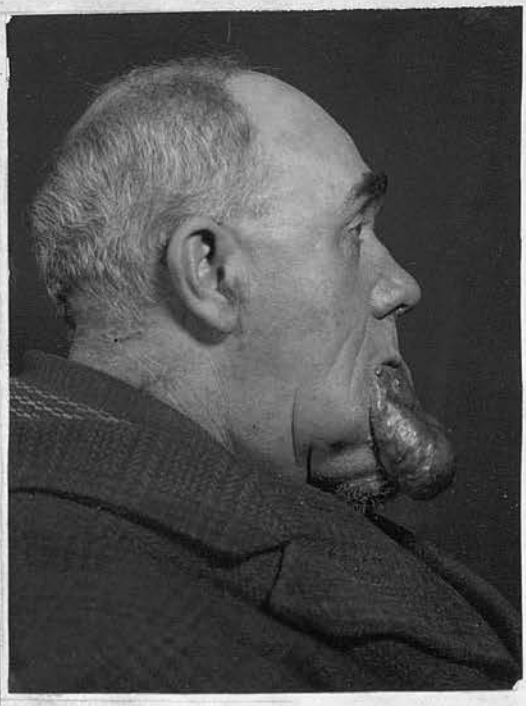
It will be noted that all the above authors believed the lesions to be in the nature of vascular malformations, not tumours. Duncan (10) wrote extensively on the subject of angioma but did not lay much emphasis on the underlying pathology. Laird (1941) (103), under the title of deep cavernous haemangioma, described a case very similar to my own, in which blood was aspirated from the swelling. He excised a tortuous, cirsoid mass of vessels, containing phleboliths, and histological examination revealed many vascular spaces, without evidence of tumour formation.

Many other authors have written extensively on blood vessel tumours which were in no way different from the vascular malformations mentioned above; full reference will be made to them in a later section. For example, Watson and McCarthy (1940)(164) gave a long account of angiomata and five cases have been quoted by me in the presentation of previously reported cases. In the first of these, histological examination of a cirsoid pulsating mass of the upper lip showed thin-walled vessels communicating with an arteriole with cellular proliferation in its walls; there was no actual proof of tumour growth.

Another important point in the management of this case was the condition of the teeth. All the teeth present were grossly carious and those in the lower jaw were almost completely enveloped in the hypertrophied vascular mucous membrane. X-Ray examination showed extensive destruction of the crowns and roots. There was thus a considerable risk of infection spreading from the tooth and producing a complication such as an alveolar abscess. Fortunately, this did not arise and it was deemed wiser not to interfere with the teeth. A difficult situation would have arisen, however, if dental extraction had ever become necessary, in view of the possibility of the vascular abnormality actually involving the mandible as well as the soft parts. Severe haemorrhage would then have been anticipated with certainty, as has been reported in similar circumstances. Broderick and Round (1933) (48) reported two cases of cirsoid aneurysm of the maxilla, of greater severity than this case and with marked pulsations present. Severe haemorrhage occurred before and after dental extraction and ligation of the common carotid artery was necessary to control it, death taking place, however, in the first case, and a successful result in the second. Bower, Ditkowsky, Klien and Bronstein (1942)(111) published details of an arterio-venous angioma of the mandible, the soft tissues of the face and the retina on one side; no dental extractions had been necessary when examined at the age of nine, though haemorrhage was to be feared.

To summarise, a report has been given of a case, illustrating the features of multiple arterio-venous fistulae of the neck.





Figs. 26, 27, & 28, Case 6. Huge size of tongue and lower lip; swelling of face and neck; many varicosities.

Figs. 29 & 30, Case 6. X-Ray film - large number of phleboliths; atrophy of mandible; gross dental caries.

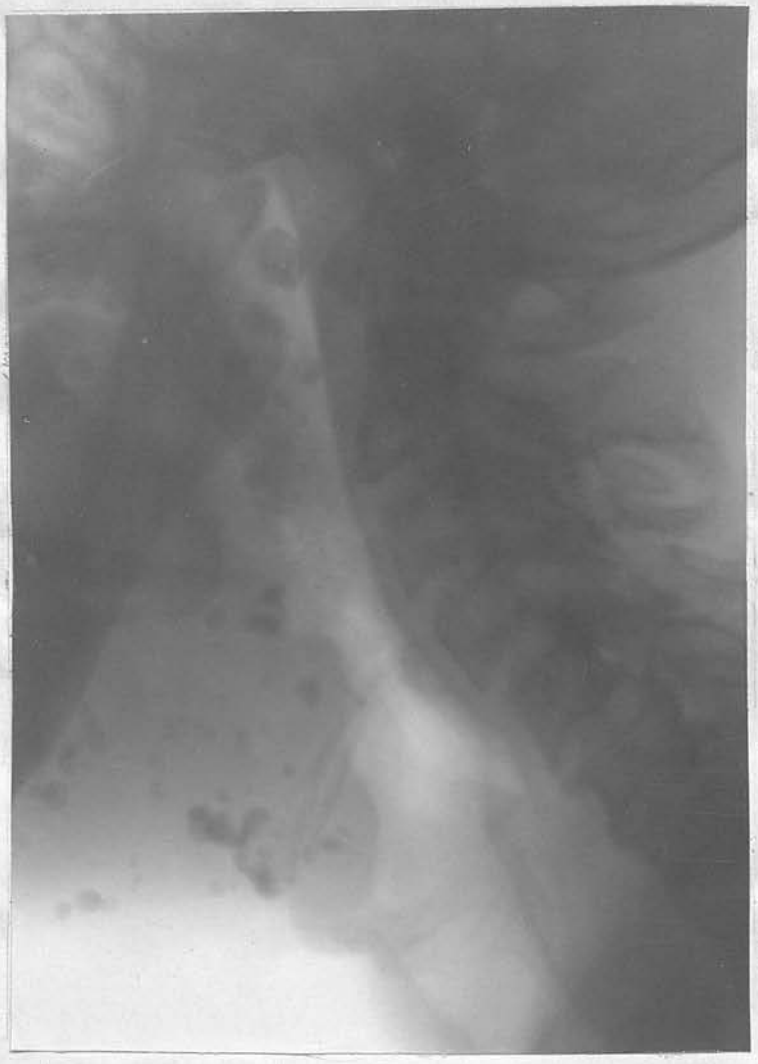


Fig. 31, Case 6. X-Ray film - large amount of phleboliths; soft tissue outline of lesion visible.

CASE 7.

J. A. Female Aged 21.

HISTORY.

The patient was born with a blue discolouration of the left eyelids and the left shoulder. Rapid spread took place thereafter, so that the whole limb and much of the face became involved in what was generally believed to be a haemangioma. Between the ages of three and five, at least three operations were carried out on the mouth, but were either of limited scope or were abandoned because of severe haemorrhage. At the age of seventeen, considerable difficulty in breathing developed, probably due to congestion of a haemangioma of the pharynx. About the same time, attacks of somnolence were noted, a disturbance of the hypothalamus being suggested as the cause. At different times between the ages of five and eighteen, courses of X-Ray treatment were given to the left upper limb, the face, the mouth and the pharynx. In the last situation, it produced great improvement in the respiratory difficulty.

CLINICAL FEATURES.

Size and Function of the Left Upper Limb.

The limb was considerably shorter than the opposite healthy limb, the humerus being $\frac{1}{2}$ inch and the radius and ulna 1 inch less. The entire shoulder girdle seemed greatly wasted, due to poor development of the pectoral and scapular muscles. When dependent, the limb became grossly engorged with blood, giving it an irregular, swollen appearance, and the circumferences at different levels approached those of the healthy limb. On elevation, the limb shrank in size due to the drainage of blood out of it, and the circumferences then became as much as $1\frac{1}{2}$ inches less than on dependency. The bones of the limb were thin, and could be easily palpated, giving the impression that little normal muscular tissue was present. The hand and fingers in particular were soft, compressible and flabby. In spite of its grossly deformed appearance, the function of the limb was surprisingly good, with satisfactory movements of all joints and a fairly strong grip of the hand. In comparison, the right upper limb was normal and both lower limbs were normal, except for a moderate degree of pes cavus.

Varicose Veins and Angiomata.

The left upper limb was the site of enormous tortuous /

tortuous distended veins, stretching from the shoulder girdle to the fingers. The obvious veins were lying subcutaneously, but many more were situated deep to the deep fascia. Most of the bulk of the limb was occupied by the veins, making all the soft tissues unduly soft and compressible and allowing easy palpation of the bones. Some of the most superficial veins took the form of large, prominent bullae, which were covered by only a thin layer of attenuated skin and seemed on the verge of rupturing. Large patches of dark blue discolouration of the skin were present over the anterior surfaces of the shoulder, elbow and hand. In the shoulder region, and especially overlying the scapula, the venous dilatations were less, but there were multiple,red, telangiectatic spots, presumed to be the result of previous X-Ray treatment.

The right upper limb was normal, except that there was a localised collection of dilated veins, moderate in size, on the posterior wall of the axilla. On the plantar surface of the second toe of the left foot there was a small dull blue area made up of a plexus of small veins. Otherwise both lower limbs were free from varicose veins or angiomata.

The face had rather an unusual appearance, being swollen and having a peculiar, patchy, blue discolouration. When the patient strained, these features were accentuated, and when she became excited or bad tempered the blue discolouration became quite severe. In the region of the left angle of the mouth, on the forehead, and on and around all four eyelids were numerous large, dilated veins and telangiectatic, blue spots. The interior of the oral cavity and the easily examined parts of the pharynx were extensively involved in reddish-blue, irregular venous dilatations. On both sides of the neck there were patches of blue discolouration and many dilated veins, most marked in the left supraclavicular region.

The left labium majus was greatly hypertrophied and the right rather less so, due chiefly to enormous, distended veins. The distended veins and blue discolouration also affected all parts of the vulva and extended far up the vagina.

Phleboliths.

Numerous phleboliths were scattered diffusely throughout the left upper limb, the face and the neck, and varied considerably in size. A few were very large and tender, the most conspicuous being one in the region of the left angle of the mandible. The X-Ray appearances were characteristic.

Local /

Local Circulatory Effects.

The circulation in the left upper limb was adequate and there was no evidence of ulceration at any point. A few attacks of phlebitis had been present in the past, but not recently. No spontaneous haemorrhage had occurred. In none of the affected parts was there any abnormal pulsation in the veins, nor any abnormal thrill or bruit. Circulatory changes, either engorgement or phlebitis, in the veins of the lesion in the neck and pharynx, had apparently given rise in the past to severe respiratory difficulty.

General Cardio-Vascular Effects.

The pulse was regular and its rate was 82 per minute when resting. On standing up, it rose to 91 per minute, but no fainting took place. On compression of the left axillary artery, while at rest, the rate dropped to 76 per minute, thus showing a positive Nicoladoni bradycardia re-action. The heart was of normal size and there were no abnormal bruits.

SPECIAL EXAMINATIONS.

Oxygen Content of Venous Blood.

A sample of blood, collected from a superficial vein of the left forearm, showed an oxygen content of 11.7 volumes %, which was quite within the normal range for venous blood. Arrangements were made for the test to be repeated, using the fractional method of obtaining specimens which had proved so important in Case 4. It was probable that a high reading would have been obtained from blood withdrawn from a vein in the arm, but, owing to unforseen circumstances, the examination was never completed.

Skin Temperature Test.

The skin of the left upper limb was warmer to the touch than any other part of the body. The accurate method of obtaining skin temperature readings was unfortunately prevented from being carried out.

Straight X-Ray Examination.

Left upper limb. All the bones were thin, poorly developed, and shorter than those of the normal limb. The only pathological change in the architecture of the bones was a slight degree of cyst-like change in the ulna, which was presumed to be due to large, irregular vascular channels traversing the bone. Many phleboliths were present in the soft tissues, almost all in the region of the elbow and forearm and a few in /

in the arm and axilla.

Head and neck. The cranium and jaws were thin and poorly developed, most markedly in the frontal region, where rarified areas were conspicuous. In the left frontal bone, one large area of rarefaction was subsequently shown at post mortem examination to be an actual perforation of the bone. Several phleboliths were present, the largest being an easily palpable one overlying the left angle of the mandible. This showed a definite concentric structure, due to the laying down of successive layers of calcium.

Arteriography.

This test was not attempted. It would have been impossible to inject the brachial artery directly by a needle passed through the skin. The alternative method of operative exposure of the artery would have entailed a difficult dissection through intensely vascular tissues and was not justifiable.

Venography.

This test was carried out by injecting Perabrodil 35% into a prominent vein in the region of the elbow, after which an immediate X-Ray exposure was made. The resulting venogram showed the large tortuous veins and venous sacs but it did not give any important information. 15 c.cs of the solution were used, but it would have taken a much larger quantity to visualise all the dilated veins successfully. Definite cramp-like pain was produced by the injection but passed off in about ten minutes.

SUBSEQUENT COURSE.

While I was still engaged in the completion of the investigation and examinations already reported, the patient suddenly developed acute mania, and was admitted at once to the Royal Edinburgh Hospital for Mental Disorders. There had been no previous history of mental disease, except that the patient was always highly strung and nervous and that attacks of somnolence had been noted a few years before.

The mania was of a severe type, with the patient extremely talkative and noisy, and using much bad language. In the first three days of the illness, there were three fits, which produced complete loss of consciousness, but were without any definite localising features. During a fit, all the dilated veins became engorged and the colour of the patches of blue discolouration was increased in intensity.

The /

The face and eyelids in particular became very swollen and cyanotic, giving the patient a most startling appearance. At the same time, there was considerable difficulty in respiration, aggravated possibly by congestion involving large veins of the pharynx. Apart from the fits, there were a few occasions when the patient flew into an extreme rage. Other unusual features were the presence of bi-lateral knee and ankle clonus and a bi-lateral Babinski sign. There was no abnormality of the eyes.

Less than three weeks after the onset of the mania, the patient died in a condition of status epilepticus.

PATHOLOGICAL EXAMINATION.

Post Mortem Examination.

Death having taken place in a mental hospital in which I had no authority, the post-mortem examination was carried out without my knowledge and was chiefly focussed upon the central nervous system. Some very desirable and important investigations of the left upper limb were thus omitted. One of these would have been the injection into the subclavian or axillary artery of one of several possible preparations. A radio-opaque preparation followed by X-Ray examination would have visualised the arterial tree and any abnormal arterio-venous connections. A non radio-opaque preparation would have given information in a different way, for example, starch would have passed from arteries into veins through abnormal arterio-venous communications but not through normal capillaries. Other examinations of the limb would have been the careful dissection of the main vessels and muscles, and histological examination of the abnormal architecture of the ulna.

However, through the kindness of Dr. W. Blackwood of the Department of Neuro-Pathology, Royal Infirmary, Edinburgh, I was given every facility for examining the various specimens removed at post-mortem examination. For the naked eye and microscopic photographs here reproduced, I am also indebted to him. In brief, the examination showed a state of what is generally called diffuse angiomatosis.

Neuro-Vascular Bundle from the Left Axilla.

The specimen consisted of a segment five inches long, removed from the axilla, and composed of the axillary artery, its branches, its accompanying veins, the three cords of the brachial plexus, and their terminal branches.

The /

The naked eye appearances were outstanding. The artery was slightly dilated, but the distribution of its branches was quite abnormal. Instead of branches such as the anterior and posterior humeral circumflex and subscapular arteries, there were seven abnormal structures, which, leaving the axillary artery, passed no further than the limits of the specimen and became intimately associated with the surrounding veins. Two very large, dilated, thin-walled veins accompanied the artery throughout the length of the specimen, and there was an innumerable collection of smaller, thin-walled veins, which intercommunicated in a most complicated, indescribable manner. The nerve trunks were of normal size and distribution, but were inextricably surrounded by the venous plexus. Small veins also infiltrated the substance of the nerves, so that the entire specimen showed a dark blue discolouration.

Careful dissection showed the following distribution of the branches of the axillary artery. The first, third and fifth arteries passed directly to end in the large veins. The second artery was the largest and soon broke up into four divisions, two passing directly into a large vein and two terminating in the plexus of small veins. The fourth and sixth arteries ended in this plexus and the seventh artery broke up into divisions which did likewise.

Microscopic examinations were made. A cross section of the whole specimen showed the same structures as naked eye examination. The axillary artery showed no abnormality in its walls. The veins were very thin-walled and seemed to be almost completely devoid of any muscle. The endothelial lining was quite normal and there was no evidence of endothelial proliferation. There was a complete absence of any sign of tumour formation.

In addition, one branch of the axillary artery was carefully dissected out as it ran towards a vein and many longitudinal serial sections were made. Microscopic examination of these failed to show any convincing arterio-venous communication, perhaps due to the tortuous course of the vessels.

Skin and Subcutaneous Tissues from Left Arm.

The naked eye changes were not so prominent as during life owing to the collapse of the large veins. The skin was normal and the large veins were the only unusual feature.

On microscopic examination, in the deeper layers of the dermis and in the underlying fat, there were /

were many large vascular spaces. The walls were chiefly composed to fibro-elastic tissue and the lining was a single layer of flattened endothelium. There was a complete absence of any evidence of tumour growth.

Muscle - The Left Biceps Brachii and the Quadratus Lumborum.

Portions of these muscles were examined. On naked eye inspection, the muscles were diffusely infiltrated by a dark blue honeycomb-like structure, which appeared to be large veins and blood spaces.

Microscopic examination again showed many large vascular spaces with a fibro-elastic wall and a lining of a single layer of flattened endothelium. There was once more a complete absence of tumour growth.

Pharynx, Aesophagus and Pericardium.

Enormous varices were found in the wall of the pharynx and aesophagus on naked eye examination. They protruded into the lumen, even when collapsed after death, and they must have been greatly distended and engorged during life. The mucous membrane was quite blue in colour as a result of the dilated veins. Numerous blue areas, composed of dilated veins, were scattered over the pericardium. Anté-mortem thrombi were common.

Microscopic examination of the aesophagus revealed collections of large vascular spaces in all the layers but mostly in the submucous coat. The walls were composed of fibro-elastic tissue and the lining was a single layer of flattened endothelium. There was no endothelial proliferation nor evidence of tumour formation.

Brain.

Naked eye appearances. There was well marked hydrocephalus of the lateral and third ventricles, but the aqueduct of Sylvius, though narrow, was quite patent. Diffusely in the white matter, but especially in the frontal areas and on the right side, the blood vessels were of larger calibre than normal. Occasionally a large vessel was found to run from the pia-arachnoid directly through the cortex into the white matter, where it pursued a course towards the ventricles. On the right side, in the white matter deep to the cortex of the hippocampal gyrus, was a small gelatinous cystic area.

Microscopic appearances. The chief feature was the presence of abnormal vessels in the brain, mentioned /

mentioned above. One type connected the veins of the white matter with those of the pia-arachnoid, and, though the direction of flow was unknown, it might well have been peripheral. Such a vein had a thin cellular connective tissue wall and was lined by a single layer of flattened endothelium. In addition, there were many large vessels of a similar structure which started near the cortex by the confluence of smaller vessels, rapidly became large and ran towards the central Galenic veins. Pickworth preparations, in addition to the above, showed in many cortical areas, firstly, that there was no obvious decrease in the density of the capillary bed, and, secondly, that though many arterioles entered the cortex to supply it and/or the underlying white matter, there were very few peripherally flowing venules. The cystic area in the right hippocampal region consisted of large thin-walled blood vessels with some loose surrounding adventitia. The appearances of the cortex elsewhere and of the basal ganglia and medulla suggested a moderate degree of cerebral anoxemia. There was an absence of any angiomatous malformation on the surface of the brain or in the membranes, and there was no abnormal calcification.

Thus, no organic blockage was found to account for the hydrocephalus. This must, therefore, be presumed to be secondary to cerebral atrophy, itself the result of an abnormal vascular system.

Spinal Cord.

Naked eye appearances. There was a definite increase in the tortuosity of the posterior longitudinal vein. In the lower dorsal region on the left side, there was a marked varicosity within the substance of the cord and also superficial to the dura mater. Higher up in the cord, the grey matter was more vascular than normal.

On microscopic examination, the dura mater of the lower dorsal region was found to contain and to surround large thin-walled blood channels.

COMMENT.

This was a very striking case, with evidence of a vascular abnormality, which was widespread and affected, in varying degrees, three limbs, the head and neck, the thorax and the external genitalia. The congenital nature was definite and, though only two small lesions, on the left shoulder and left eyelids, were noticed at birth, spread took place rapidly and apparently /

apparently almost reached its maximum by the age of three. Full investigations were being carried out when the sudden onset of mania caused them to be abandoned. At the post-mortem examination, attention was unfortunately not directed to the left upper limb as completely as was desirable. A fuller discussion on many of the points to be mentioned will be given in a later section.

The diagnosis of the state of the left upper limb was perhaps at first sight debatable. In the past, a haemangioma had generally been considered the cause, but it seemed quite probable, by comparison with other reported cases, that a vascular abnormality might be present, either phlebectasis or arterio-venous fistulae. The exact relationship of these three conditions is admittedly confused, as seen by references in the literature. The very prominent dilated veins were typical enough of phlebectasis, but could conceivably have been associated with arterio-venous fistulae, in spite of the absence of a thrill, a bruit or abnormal pulsations. The test for the oxygen content of venous blood did not give a conclusive result, and it was not possible to have it repeated. It was intended to carry out the method advised by Veal and McCord (57), in which several tourniquets were applied to the limb and blood was withdrawn from the segments of veins thus isolated. It was highly probable that the venous blood in the upper part of the arm would have shown a high oxygen content.

The stunting of the limb was unusual, as most examples of similar vascular lesions have been associated rather with hypertrophy. Reid (1931)(76), however, reported a venous angioma of the lower limb in which there was a decrease in size. In the present case, there seemed no doubt that the small size of the limb could be traced to the previous intensive X-Ray treatment, which had so severely damaged the epiphyseal cartilages that further growth became restricted. It was impossible to decide if hypertrophy would have developed had the treatment not been carried out.

The phleboliths and the changes in the structure of the ulna were features often noted in vascular abnormalities, and Case 8 will be seen to demonstrate both more completely. Venography was not found to be of importance, though Fulton and Sosman (1942)(110) believed the results in similar cases to be indicative of angioma of muscle.

The pathological examination revealed a peculiar development of the branches of the axillary artery, which, after a tedious dissection, were seen to /

to pass directly into the very large plexus of veins lying around the artery. There was thus conclusive evidence of multiple small arterio-venous fistulae. Microscopic examination did not demonstrate the actual fistulous communications, but it showed for certainty that the veins were of normal structure and that no tumour growth was present. The relationship of the veins to the brachial plexus was outstanding, as the veins completely surrounded the nerves and were also present in the substance of the nerves. Stewart and Bettin (1924)(24) described a case in which the popliteal nerves were similarly affected by an angioma, though proof of the neoplastic origin of the disease was lacking.

The lesions visible in the other parts were similar to those in the left upper limb. The large veins and blue discolourations of the face, in particular, gave an unsightly appearance, which was accentuated by any straining or excitement. It could not be decided whether these scattered lesions were purely venous in character, or were due to arterio-venous fistulae. Naked eye pathological examination of the pharynx and aesophagus revealed an extraordinary degree of varicosities, similar to those of the left upper limb and face. Microscopic examination of the aesophageal wall showed very large veins but there was no proof of arterio-venous fistulae and there was no sign of tumour growth. The specimens of muscle examined showed merely dilated veins and blood spaces.

With the onset of mania, a new line of investigation was opened up. The mania was perhaps unconnected with the other lesions but it did seem possible that an intracranial vascular abnormality might co-exist. The condition chiefly to be considered was a rare one, with several names, of which Sturge-Weber disease was perhaps the best known. Briefly, this condition is characterised by a facial haemangioma, typically confined to one or more divisions of the trigeminal nerve, angiomatous changes in the vessels of the pia mater, mental changes, abnormal intracranial calcification, and congenital glaucoma. Atypical varieties were known to exist in which one or more of the above features was absent, and it was felt that the present case might be some such unusual type. Good accounts of the condition have been given by Parkes Weber (118) and (119), and Nussey and Miller (125). Newson (1939)(80) described a case of Sturge-Weber disease, with a resemblance to the present case in that there were signs of arterio-venous fistula of an upper limb. Northfield (1940-1) (126) also reported a combination of lesions of a similar nature in a boy of nine years.

In the present case, the facial angiomata

were /

were widespread and not confined to the distribution of one nerve, both eyes were normal, but interesting intracranial vascular changes were found post-mortem, though there was neither an angiomatous malformation nor any abnormal calcification. The cerebral abnormality consisted of a peculiar development of the veins between the white matter and the pia-arachnoid, and between the cortex and the central Galenic veins. This subject, however, was beyond the scope of the thesis, and a full account of the cerebral condition is expected to be published independently by Dr. W. B lackwood. Varicosities were also found in relation to the spinal cord. The presence of knee and ankle clonus and Babinski's sign were no doubt the result of these varicosities.

In summarising the findings in this case, the widespread nature of the vascular abnormality might have suggested a diagnosis of multiple angiomatosis, by which term a true tumour should be indicated. In no situation, however, was there any evidence of tumour formation, and there could be ruled out the one possibility of a single lesion being a primary and the others metastatic lesions, and also another possibility of multiple independent primary tumours. The condition, therefore, could be correctly considered as a widespread abnormality in the development of the blood vascular system, showing itself in many regions of the body and in many different tissues, such as skin, subcutaneous tissues, muscle, nervous tissue, bone, serous and mucous membranes. The exact nature of the abnormality probably varied. In the left upper limb, there were definite multiple small arterio-venous fistulae with an excessive formation of the veins. In all the other parts examined, such fistulae were not demonstrated and the lesions were believed to be purely venous in nature.

APPENDIX.

At this point, the opportunity will be taken of quoting the case of a female, K.R., aged 16, who attended the Royal Infirmary, Edinburgh, in 1935, whom I did not have the opportunity of examining, but to whose records I have had access. There was a history that, since birth, purple marks had existed on the left upper and lower limbs and the left side of the trunk. At the age of seven, a vein had been excised from the left leg, along with some of the birthmarks, and a lesion on the left wrist had also been treated with radium. On examination in 1935, the appearances were those of capillary and cavernous haemangiomata, widely scattered but strictly limited to the one side. At operation then, a large portion of the lesion was excised from the left calf, and a course of X-Ray treatment followed. Soon afterwards the patient left the district and did not attend for further examination.

The final report on the case came to my notice in 1941. It appeared that, earlier that year, she was admitted to a hospital in England, suffering from a sudden paraplegia which soon proved fatal. Post-mortem examination showed many haemangiomata in the spinal cord, presumably the cause of death.

Unfortunately, it has not been possible to trace any more detailed records of the various pathological examinations. The clinical records were also brief, with no mention of the various methods of examination now considered important, nor any note on the relative size of the limbs. It is, therefore, impossible to give an accurate diagnosis but it is likely that phlebectasis was present and perhaps arteriovenous fistulae, more particularly in the lower limb. The clinical appearances were, therefore, similar to those of my own case. In both cases, the original lesions appeared to be confined to the situations obviously visible, but in both there was the sudden, serious onset of clinical features referable to some central nervous system disorder, which was soon fatal. An important point, in view of these facts, is that vascular abnormalities in the brain or spinal cord or their membranes should be suspected, more frequently than is general, in any case showing obvious lesions of a severe nature in any part of the body. The possibility of such changes, therefore, must make the prognosis guarded but difficult to estimate, and in neither of these two cases was there any definite indication that death would occur so suddenly.

Figs. 32 & 33, Case 7. Intense venous engorgement of upper limb on dependency; dusky discolouration of limb, neck and face due to haemangiomata and large veins; telangiectases.

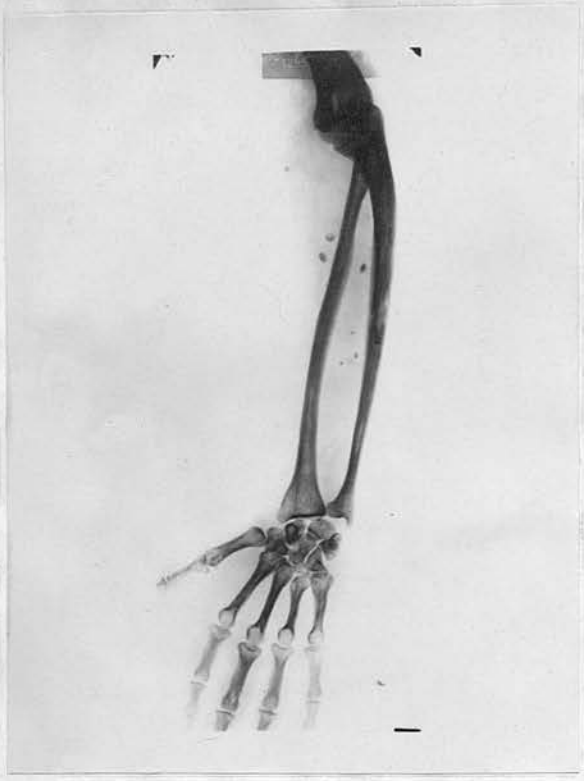


Fig. 34, Case 7. X-Ray film - a few phleboliths; slender atrophied bones; structural changes in shaft of ulna due to enlarged vascular channels.

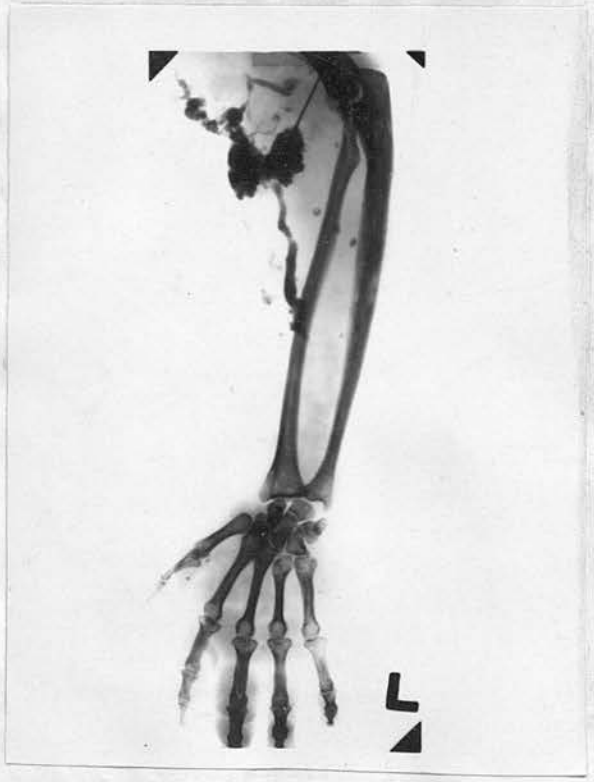


Fig. 35, Case 7. Venogram - greatly dilated tortuous veins, difficult to fill adequately with opaque medium.

Figs. 36 & 37, Case 7. X-Ray films - atrophy of cranium and jaws; large phlebolith at angle of left mandible (posterior view).

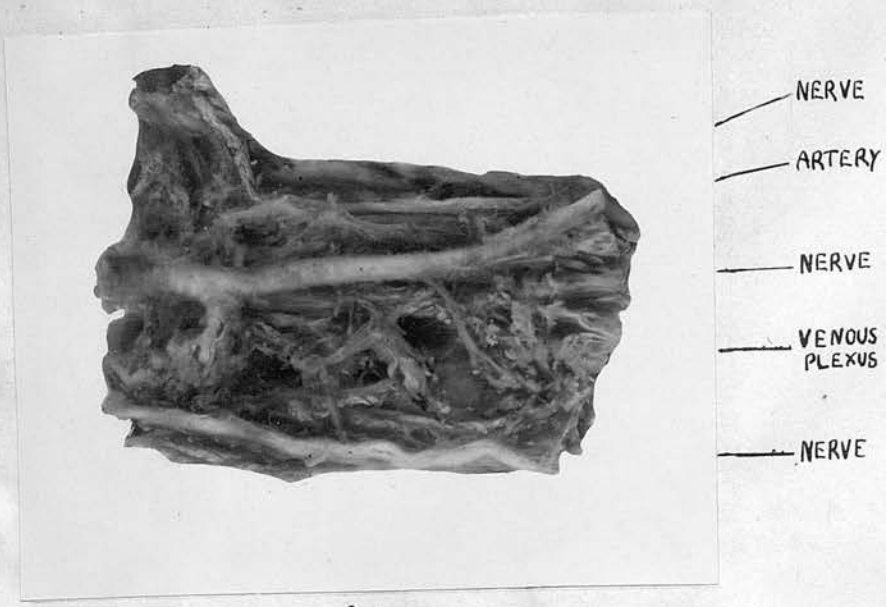


Fig. 38, Case 7. Pathological specimen, naked eye - neurovascular bundle from axilla, showing artery, nerves and large venous plexus.

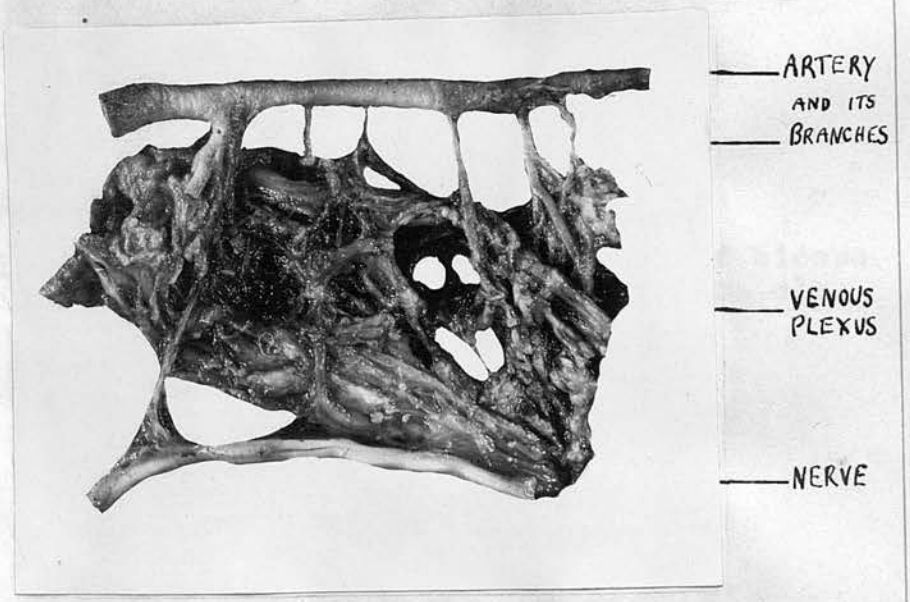


Fig. 39, Case 7. Pathological specimen, naked eye - after dissection of neurovascular bundle from axilla, showing branches of artery passing into venous plexus.

Fig. 40, Case 7. Microscopic section, LP, of skin and subcutaneous tissues,—large vascular spaces.

Fig. 41, Case 7. Microscopic section, LP, of biceps brachii - large vascular spaces and normal muscle.

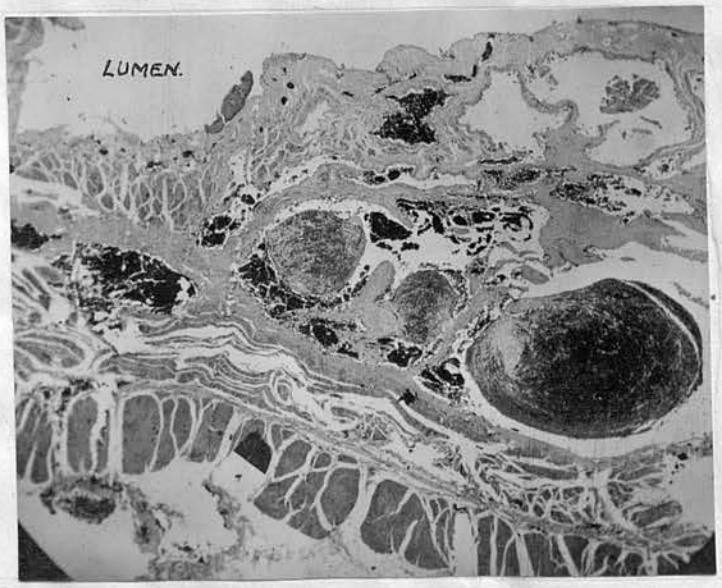


Fig. 42, Case 7. Microscopic section, LP, of aesophagus - large vascular spaces in submucous coat.

CASE 8.

P.H. Male. Aged 16.

HISTORY.

At birth, blue swellings were present on the palmar surface of the third finger of the right hand and on the back of the right shoulder. As the child grew during the next few years, the entire upper limb became involved in blue swellings which seemed to be chiefly large veins. From infancy onwards to the age of twelve, this unfortunate child spent long periods in different hospitals, either for treatment of the original lesion, or on account of complications. He was quite intelligent, though had obviously suffered from the interrupted education.

The following are some of the more important points in the history. In infancy, an operation was performed on the right third finger, which thereafter grew more slowly than the others. Severe bleeding sometimes took place from the veins after an injury to the limb. At about the age of nine, the lesion was progressing fairly rapidly and it was feared that amputation might be necessary. X-Ray treatment had been given three years previously, and it was now repeated on an intensive scale with the result that spread was arrested. Further courses were given four and five years later.

On more than one occasion, septic phlebitis developed, giving rise to abscesses in the limb, which required incisions for their drainage, the pus obtained showing a pure culture of haemolytic streptococci. At the age of eleven, an attack of phlebitis gave rise to a severe type of septic broncho-pneumonia, from which the boy recovered after a prolonged illness. Simultaneously, acute arthritis of the wrist occurred, due to a haemolytic streptococcal infection.

Other operations had been carried out at different times, without success, such as local excision and ligation of veins and puncture with the cautery. Ultimately, the affected limb became much smaller than the opposite limb. Pain was absent except during the attacks of phlebitis.

CLINICAL FEATURES.

Varicose Veins and Angiomata.

The right upper limb was affected by a most striking /

striking abnormality, as it was short and showed a tremendous development of the veins. These veins formed a huge plexus of tortuous dilated vessels, involving the entire limb from shoulder girdle to fingers and causing great irregularity of the surface of the skin. Many were very superficial, bulging through the skin as bullous dilatations and covered by only a thin layer of skin. Others were more deeply placed and covered by bluish discoloured skin. In the scapular, pectoral and shoulder regions, the dilated veins were less prominent, but there was an extensive formation of telangiectases, fairly typical of the type produced as an end result of intensive X-Ray treatment. No superficial or capillary naevus was present, though the whole limb showed a marked, bluish discolouration.

A small bluish mark, about $\frac{1}{8}$inch in diameter, was present on the right side of the bridge of the nose and appeared to be a localised venous dilatation. It was painless, soft and compressible, and occasionally gave rise to severe haemorrhage when injured.

Phleboliths.

Numerous phleboliths were present throughout the right upper limb and formed hard, sometimes tender, nodules. They were probably the result of previous phlebitis. The X-Ray appearances were outstanding and typical.

Size and Function of the Right Upper Limb.

There was a great disparity in the size of the upper limbs, the right, abnormal one being smaller in every respect. On elevation of the limb, it was seen to be very thin and there seemed to be little thickness of tissue between the skin and the bones. On dependency, it became greatly engorged by filling of the large veins, giving the limb a very swollen appearance, though in actual fact, it was still smaller than the normal limb. Considerable atrophy of the limb was, therefore, present and was most noticeable in the shoulder region where the swelling was slight. The principal measurements were as follows:-

Lengths.	Right Upper Limb.	Left Upper Limb.
Tip of acromium - lateral epicondyle.	12 inches.	$13\frac{1}{2}$ inches.
Olecranon - ulnar styloid.	7 "	$10\frac{1}{2}$ "
Head of radius - radial styloid.	$9\frac{1}{2}$ "	$11\frac{1}{2}$ "
Thumb.	$1\frac{3}{4}$ "	$2\frac{1}{2}$ "
Third finger.	$2\frac{1}{2}$ "	$3\frac{3}{4}$ "
Fourth finger.	$2\frac{1}{2}$ "	$3\frac{1}{2}$ "

Circumferences. /

Circumferences	Right upper limb. elevated.	Right upper limb. dependent.	Left upper limb.
Middle of arm.	6 inches.	$6\frac{1}{2}$ inches.	$8\frac{1}{2}$ ins.
Middle of forearm.	$4\frac{1}{2}$ "	$5\frac{3}{4}$ "	$7\frac{1}{2}$ "
Wrist.	6 "	7 "	$6\frac{1}{2}$ "
Metacarpal heads.	$6\frac{1}{2}$ "	$6\frac{3}{4}$ "	$7\frac{1}{2}$ "
Fourth finger.	2 "	$2\frac{1}{2}$ "	$2\frac{1}{2}$ "

It was thus noted that, though all the bones in the right upper limb were smaller than those in the left, the ulna was much shorter than the radius. As will be discussed later, the stunting of the limb was believed to be due to the previous X-Ray treatment, which had damaged the epiphyseal cartilages and interfered with subsequent growth. The ulna had suffered more than the radius, and, at the lower end, its epiphysis was more poorly developed than that of the radius. The X-Ray treatment had started at the age of six, when the ulnar epiphysis was beginning to appear, whereas the radial epiphysis had been present for three or four years before that. Probably these facts accounted for the difference in growth of the two bones. There thus resulted a fairly severe manus varus deformity; that is with the hand deviated towards the ulnar side.

The function of the limb was surprisingly good, considering its grossly abnormal appearance. The only severe restriction of movement was at the elbow joint, where merely 120° of extension and 70° of flexion were possible, due both to the presence of scars of old incisions which had become tightly contracted, and to the previous infection in the region. The fingers had a full range of movement, but the grip was weak. There was, however, a considerable reluctance to use the limb, and with more practice and perseverence there was little doubt that an improvement in function could be produced.

Local Circulatory Effects.

The circulation of the limb was good and there was no evidence of ulceration or commencing gangrene. There was no abnormal pulsation in the veins nor any palpable thrill nor audible bruit over arteries or veins. Several attacks of phlebitis had taken place in the past, usually of an acutely infective nature. An interesting point was that these had produced thrombosis in many of the veins, leading to a certain degree of spontaneous improvement in the lesion.

An attempt was made, as in Case 1, to determine roughly the amount of blood which passed into the veins /

veins in the right upper limb. A tourniquet was applied as high in the arm as possible so as to prevent filling of the large veins. On its release, water was displaced from a tank in which the arm was immersed and its amount indicated roughly the volume of blood which passed into the veins. The reading was 350 c.cs showing a considerable loss of blood from the general circulation.

General Cardio-Vascular Effects.

The pulse rate at rest was 60 per minute, and on compression of the right brachial artery, it dropped to 52, indicating a positive Nicoladoni bradycardia reaction. On standing up from a resting position, the pulse rate rose to 70 per minute. The blood pressure measured in both arms was 80/55. No cardiac abnormality was detected.

SPECIAL EXAMINATIONS.

Skin Temperature Test.

Measurements were taken at corresponding points on the anterior surfaces of the upper limbs, at an average room temperature of 19.5°C.

	Right.	Left.
Shoulder	32°C	30°C
Mid-arm	32.2	27.5
Elbow	30.5	28.5
Mid forearm	32	30.2
Wrist	31.7	25.8
Thumb	34.2	28.8
Middle finger	32.5	28.5
Little finger	33.5	29

It was evident that there was a considerable increase in the temperature of the right upper limb. This could be accounted for by the degree of venous congestion alone and not necessarily by an arterio-venous communication.

Oxygen Content of the Venous Blood.

Blood was withdrawn from superficial veins on the anterior aspects of the elbows, using the usual technique, and it was noted that the specimen from the right side was bright red in colour. Estimation of the oxygen content showed readings of 9.1 volumes % on the left side and 15.5 volumes % on the right. This difference showed conclusively that one or more abnormal arterio-venous communications existed in the right upper /

upper limb.

Straight X-Ray Examination.

Several important abnormalities were present. All the bones of the right upper limb were short, frail and decalcified, and it was believed that the previous intense X-Ray treatment had damaged the epiphyseal cartilages so that further growth was restricted. This effect was most noticeable at the wrist, where the lower epiphysis of the ulna had not developed as much as that of the radius, so that a pronounced manus varus deformity was produced. There were changes of an arthritic nature in the elbow and wrist joints, and it was difficult to estimate whether they were due to X-Ray treatment or to the previous septic infections in and around the joints.

There were numerous, irregular spaces in all the bones, giving a cyst-like, vacuolated or honeycombed picture. They were believed to be due to enlarged vascular channels traversing the bones. The largest single lesion of this type was found in the lower end of the shaft of the humerus, and it gave the appearances recognised to be found in an isolated angioma of bone.

The irregular surface outline and the swelling of the soft tissues were well demonstrated. There were many phleboliths scattered throughout the limb, most being below the level of the middle of the arm. They varied in size, but some were very large. They were chiefly smooth and round, and composed of concentric circles of slightly different densities, as the result of irregular laying down of calcium.

The cranium was of small size and showed the presence of abnormally large venous channels, probably in the diploë. There was a slight degree of calcification of the pineal gland, which could not be considered an abnormal appearance.

Arteriography and Venography.

Arteriography was not attempted. Owing to the scarring on the front of the elbow, it would have been impossible to inject the brachial artery by blind puncture through the skin. Exposure of the brachial artery at operation would have called for a difficult and perhaps dangerous dissection and was not justifiable. Venography was attempted using Perabrodil 35%. A few of the enlarged veins were filled but no useful information was obtained.

PATHOLOGICAL EXAMINATION.

Biopsy.

A biopsy was carried out, a local anaesthetic being used to infiltrate a small part of the lateral side of the right arm. There was some difficulty in injecting the solution as the point of the needle pierced many veins and great care was required to be sure that none of the solution was allowed to pass into the circulation. An incision two inches long was made and a huge mass of veins was encountered on reflecting the skin. These were very friable and most severe haemorrhage took place, the blood being bright red in colour like arterial blood but not pulsating. A portion of this mass of veins was excised, and haemorrhage was finally controlled with difficulty, many ligatures being required. The skin wound was closed and a firm pressure bandage applied.

Histology.

Microscopic examination showed many veins of perfectly normal structure embedded in fibrous and fatty tissue. No evidence of haemangioblastoma was present.

DIAGNOSIS.

Clinical examination and the presence of a high oxygen content of the venous blood of the affected limb showed definite proof of the existence of arterio-venous fistulae. Pathological examination demonstrated the absence of any tumour growth and confirmed that the lesion was a vascular abnormality.

TREATMENT.

At the time I examined the patient, the condition was quiescent, and there was no call for any further treatment, either by surgery or by irradiation.

COMMENT.

The diagnosis of the lesion of the right upper limb was of considerable interest, though there was no doubt about its congenital nature. A haemangioma, indicating a true tumour, had previously been considered the cause, but it was not possible to trace thepathological records. In view of the pathological findings in Case 7, and by comparison with other recorded /

recorded cases, I believed it probable that the essential cause was not a tumour, but was a malformation of the blood vascular system in which arterio-venous fistulae were present. The abnormality was very accurately confined to the complete upper limb, including the shoulder girdle, a fact which suggested a developmental defect rather than a tumour. Two signs which were conclusive evidence of arterio-venous fistulae were the high oxygen content of the venous blood of the affected limb and the positive Nicoladoni bradycardia re-action. Their presence ruled out the closely allied condition of phlebectasis or venous angioma. The absence of any abnormal pulsation, thrill or bruit was known not to prohibit a diagnosis of arterio-venous fistulae but merely to indicate that such fistulae were small. Almost certainly also, they were multiple, as otherwise the oxygen content would not have been so high.

The frequent attacks of phlebitis of a septic nature were unusual and serious, but a satisfactory sequel was the widespread thrombosis, which was believed to have produced a degree of spontaneous arrest of the lesion at a time when it was spreading. Another result was the extensive formation of phleboliths which were easily palpable clinically and showed a most outstanding X-Ray picture.

The degree of stunting of the limb was very severe, and it was difficult to determine how much of it could be attributed to the pathological condition and how much to previous X-Ray treatment. Though most recorded cases of similar vascular abnormalities have tended to produce hypertrophy of a limb, a small number have been associated with shortening, e.g. Reid (1931)(76), but not to the extent seen here. It seemed certain, however, that the previous intensive X-Ray treatment, applied to the entire limb, had caused such destructive effects on the epiphyseal cartilages that subsequent growth became extremely restricted. Among the interesting references to this action of X-Rays on growing bone, were those of Bisgard and Hunt (140), Regen and Wilkins (141) and Barr, Lingley and Gall (142). From the history of the case, it appeared that amputation was at one time feared to be imminent and that it was prevented only by the X-Ray treatment arresting further spread. Thus the extreme stunting was the price to be paid for the saving of the limb, which actually proved later to be quite a useful member.

X-Ray examination also showed alterations in the structure of the bones, with the presence of numerous/

numerous irregular vacuoles giving a cyst-like appearance. The most probable explanation was that the bones of the limb were riddled with large venous channels containing arterial blood, and it was of interest to note also that the cranium showed unduly prominent vascular markings. Good references to these bony changes have been given by Reid, (1925)(72), Case 31 of his series, and by Dean Lewis, (1930)(41), Case 1. By some, however, such alterations in the bony structure have been designated as due to angiomata, a tumour usually being indicated. Nemenov (1939)(83) and Hirschfeld (1941)(101) were amongst those who gave that diagnosis. Other less likely causes of the bone changes were the atrophy of disuse and hyperaemic decalcification, but there was no typical feature of either.

The blue spot on the nose seemed to be composed of a small localised venous dilatation, about $\frac{1}{8}$ inch in diameter, but without any obvious superficial vessel connected with it. As the parents would not consent to any treatment being carried out, there was no opportunity of discovering the exact pathology. It might possibly have been purely venous in structure, though, on the other hand, such a mark has been known to be the first obvious feature in serious arterio-venous abnormalities. Examples of the spread which may take place from such a small lesion were to be found in the upper limb of this case, and in Case 7 of my series. In the case of Müller in 1891, quoted by Bland Sutton (127), and in those of Bernheim (1925)(25), and Wilbur (1930)(39), a spot about the same size, but red in colour, was the obvious original sign of what proved to be extensive arterio-venous fistulae.

It was possible that the lesion on the nose was an actual tumour, but it was most unlikely that this could be a manifestation secondary to a tumour in the right upper limb. Probably the two lesions arose simultaneously but independently, and, along with the large vessels of the cranium, indicated that the vascular abnormality was more widespread than was at first apparent.

A condition of a different type which might have caused the mark on the nose was a glomangioma, due to an abnormality of the neuro-myo-arterial glomus. Though the site was rare and the absence of pain uncommon, the appearance resembling a dilated vein was quite typical. This possibility was suggested in view of the findings in Case 9, and, if it were correct, the interesting problem would be raised as to whether the lesion in the upper limb might not have been due to the same cause. Microscopic examination, however, showed /

showed that that was not the case. Case 9 and the additional case there recorded will show that very rarely a glomangioma can be quite an extensive lesion. This subject will be studied more fully under Case 9 and in the discussion.

The ultimate prognosis is uncertain and must be guarded. It is possible that, even after years of relative quiescence, the lesions in the limb and face may become active and give rise to serious effects such as increase in size, abnormal pulsations, a thrill, a bruit, ulceration, haemorrhage or gangrene. There is also the risk of the occurrence of symptoms due to unexpected intracranial vascular abnormalities and those due to progressive heart failure.

The problem of treatment was always difficult and will continue to be so. Many methods have been tried in similar circumstances with very varying results. Local excision of masses of veins and their communicating arteries may be temporarily successful but a feature of the disease is the possibility of further fistulae becoming patent at a later date. A local excision in this case was carried out on the third finger in infancy, but this did not prevent rapid enlargement. X-Ray and radium treatment have their limitations and though the former certainly arrested spread, it could not be said to have produced a cure and did have serious effects on growth. A more extensive operative method would entail the wide exposure of the main arteries of the limb with ligation of all fistulous tracks, but it must obviously be a formidable and difficult procedure and one not necessarily to be followed by satisfactory results. Amputation was a method at one stage considered to be imminent and always liable to become necessary in the future should serious disturbances of circulation occur in the limb. This also would be an extremely hazardous undertaking, and to be effective even an interscapulo-thoracic amputation would scarcely be complete owing to a large part of the chest wall being involved. Berhneim (1925)(25), for example, spoke of the terrific haemorrhage at an amputation below the shoulder and certainly the biopsy carried out by me showed how severe it would be if any major procedure were attempted.

As, however, the condition is at present quiescent, it will be wise to follow the advice of Horton, quoted by Franklin (124), that operation in a severe case such as this is better avoided. Ultimately the stage might be reached when amputation would become necessary, either on account of local effects or cardiac changes.

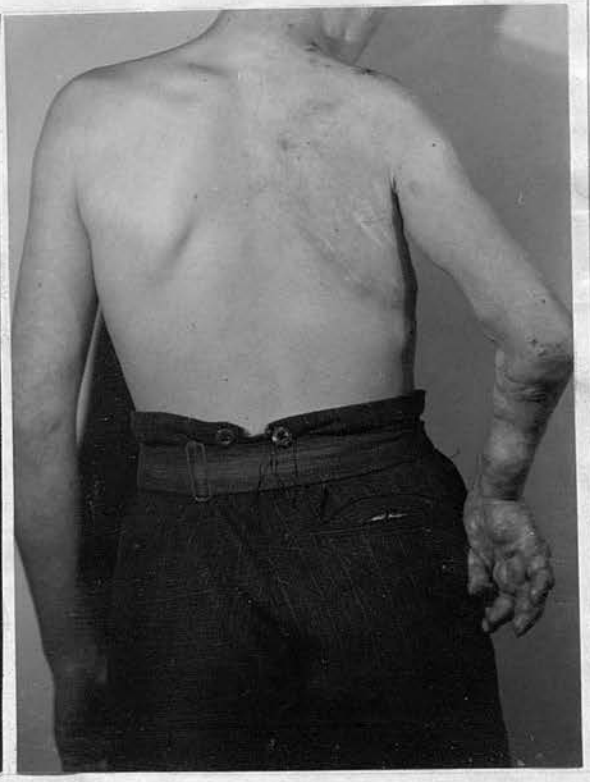
To /

To summarise, a report has been given of a case of arterio-venous fistulae of the right upper limb, associated with a small vascular abnormality of the nose.

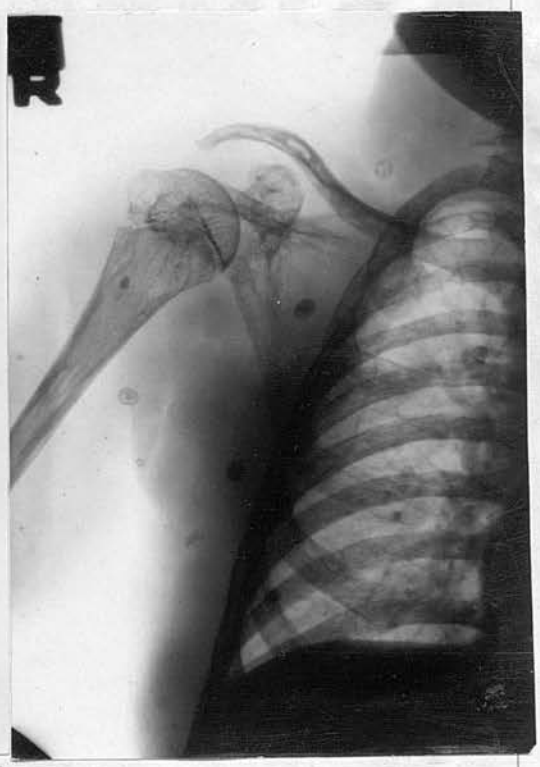
ADDITIONAL NOTE.

A year after the first examination by me, an area of redness, about one inch in diameter, appeared over the right wrist and persisted for over six weeks, in spite of suitable surgical dressings. Ulceration later developed and a greyish slough was noted in the centre. Eventually it was found easy to remove a complete phlebolith, $\frac{1}{2}$ inch in diameter, from the depths of the ulcer. Thereafter, the wound healed quickly and the surrounding area of infection settled down.

About a year and a half later, the patient received an injury to the right forearm as the result of a fairly severe fall. Extreme pain, tenderness and swelling developed at once, and X-Ray examination revealed transverse fractures, with no displacement, of the lower thirds of the radius and ulna. Treatment was by immobilisation in a light, loosely fitting plaster of Paris shell and at the end of six weeks this was discarded as union was satisfactory. At the outset there was a justifiable fear of non-union occurring, but fortunately recovery took place rapidly and without difficulty.



Figs. 43, 44 & 45, Case 8. Gross stunting of entire right upper limb, including shoulder girdle; extreme venous engorgement on dependency and irregularity of skin surface; several telangiectases; ulnar deviation of hand.



Figs. 46, 47 & 48, Case 8. X-Ray films - numerous large phleboliths; atrophy of bone and enlarged vascular channels in bone; lack of development of lower ulnar epiphysis, causing deviation of hand; irregular soft tissue outline.

CASE 9.

M. McC. Female. Aged 17.

HISTORY.

A blue spot had been present on the right wrist at birth and it had gradually become bigger to forma painless swelling. Three similar spots were present elsewhere at birth.

CLINICAL FEATURES.

On the anterior surface of the lowest quarter of the right radius there was an obvious swelling about 2 inches by $1\frac{1}{2}$ inches in size. It was soft and compressible, emptied partially on elevation of the limb, and became tense and firm on dependency. The centre of it was more prominent and dark blue in colour, forming a projection $\frac{1}{4}$ inch in diameter. This simply had the appearances of a distended vein and there was no naevus. There was an absence of any pulsation, thrill or bruit, and there was no obvious increase in the temperature of the skin overlying it. The lesion lay directly over the radial artery which appeared to be normal. There was a complete absence of pain or discomfort and the function of the limb was unimpaired. There was no abnormality in the rest of the limb, nor any disparity in the sizes of the limb.

In addition to this obvious lesion, small dark blue compressible spots, about $\frac{1}{8}$ inch in diameter, were present on the lobule of the right ear, on the sole of the right foot, and on the anterior surface of the left leg. They were painless and caused no trouble.

No cardio-vascular changes were present.

SPECIAL EXAMINATIONS.

Oxygen Content of Venous Blood.

An aspirating needle was inserted into the protuberant vein forming the blue centre of the swelling and bright red blood was withdrawn. After 2 c.cs had been obtained, the swelling collapsed but filled again in a minute, even with the limb elevated, after which more blood couldbe obtained. The oxygen content of the blood withdrawn from this superficial venous dilatation was 17.6 volumes %, a high reading, which indicated that arterial blood circulated in the veins of /

of the swelling.

Straight X-Ray Examination.

This showed the soft tissue swelling overlying the lower end of the radius. There was no abnormal bony condition.

Arteriography.

Arteriography was carried out at the same time as operative treatment and is described with the latter.

PROVISIONAL DIAGNOSIS.

In view of the fact that several of my cases of arterio-venous fistulae had started in a way similar to this case, it was thought advisable to investigate this case fully. Owing to the early stage of its development, it was hoped that light might be shed on the growth of the more severe lesions. Clinical examination naturally suggested one of the forms of congenital vascular lesion generally called an angioma, and it was obvious that the lesion consisted chiefly of a mass of dilated veins, without any actual naevus formation. The fact that the lesion filled, with the limb elevated, after its contents had once been evacuated, certainly suggested abnormal arterio-venous communications. This was made positive by the presence of a high oxygen content in the blood obtained from the abnormal veins.

OPERATION.

This was carried out entirely under local anaesthesia, using planocaine 1% with adrenalin. The incision was made along the line of the radial artery, passing at its distal end to the medial side of the lesion.

Arteriography was carried out as a preliminary step. The radial artery, of normal size, was exposed in the lowest third of the forearm above the angioma. After dissecting it up from its surroundings and retracting it with tape, 5 c.cs of Pyelectan were injected, retraction was released, and an immediate X-Ray film was taken. The opening in the artery closed spontaneously and ligation of the radial artery was not required. Scrutiny of the X-Ray films showed filling of the commencement of the cephalic and basilic veins. In addition, many small vessels were visualised in a plexus at the site of the lesion, and it seemed as though one or two of them connected the radial artery with /

with the cephalic vein.

Exploration of the Lesion was carried out at once. On dissecting at the distal end of the incision, a bunch of large fragile veins was exposed which bled copiously on separation from the attenuated skin overlying. Deep to them was a plexus of small veins. The radial artery was traced distally with care and two small branches about ½ inch long were found to leave the anterior aspect of it close together and to pass directly into the plexus of veins. These branches were ligated and divided. Several veins were also ligated and the complete mass of veins was excised. Complete haemostasis was obtained and the wound was closed.

PATHOLOGICAL EXAMINATION.

Naked Eye Appearances.

The specimen excised seemed to be nothing more than a tangled mass of veins, with the two small arteries leading into them.

Microscopic Appearances.

Histological examination rather surprisingly gave the typical picture of a glomangioma of the cavernous type. Low power magnification revealed many irregular cavernous spaces filled with blood. They were of different sizes and in places communicated with each other. A moderate amount of fibrous tissue stroma was present. High power magnification showed a single layer of flat endothelial cells lining the cavernous spaces. Immediately external to these were the cells now generally called the glomus cells or epithelioid cells arranged in parallel rows four or five deep. They were large cuboidal cells, with circular nuclei, reticular chromatin and pale rim of cytoplasm. There was no definite evidence of proliferation of nervous tissue.

SUBSEQUENT CLINICAL COURSE.

The operation wound healed without difficulty within a fortnight. Examined six weeks after operation, the scar was satisfactory and painless and the patient had no complaints.

COMMENT.

This /

This case was of most unusual interest, as it represented an early degree of a vascular abnormality and as its investigation might be expected to throw light on the development of some of the more extensive types of lesions. At birth there were four similar blue spots - on the right forearm, the lobule of the right ear, the sole of the right foot, and the left leg, of which the first alone had ultimately shown gradual increase in size. Each of the three others simply looked like a solitary dilated vein, compressible, very superficially placed and painless. The principal lesion appeared merely like a localised bunch of dilated veins, which was soft and easily emptied by pressure, to fill again in about a minute. The high oxygen content of the blood withdrawm from the most superficial part of the swelling, obviously a vein, showed the definite presence of an abnormal arterio-venous communication. Arteriography showed up the plexus of veins, and also indicated probable fistulae. On exploration of the radial artery, two small arteries were found to leave it and pass by direct continuity into the veins forming the plexus, thus proving conclusively the presence of two small arterio-venous fistulae.

Histological examination showed the surprising picture of a typical glomangioma. Clinically, the lesion did not resemble a glomangioma, as it was painless, large and not in the common situation, but it was recognised that such unusual types do occur. The subject of glomangioma will be studied in a later section in which more full references will be given. Mackey and Lendrum (148) described a similar case, Case 1 of their series, where the appearances were those of a painless localised collection of varicose veins. These veins were removed at operation, an afferent artery being demonstrated, and pathological examination revealed the presence of a glomangioma. No estimation was made of the oxygen content of the venous blood.

Harvey, Dawson and Innes (147) gave a microscopic picture of a glomangioma in figure 33 and added an interesting brief note on the clinical features. A small blue spot was present on the left wrist at birth, and from it spread took place until finally a large part of the upper limb was involved in varicose veins. Local excisions of the veins and irradiation were carried out in 1933 at the age of 18. No estimation was made of the oxygen content of the venous blood. By chance in 1942, I saw this patient, with a minor complaint of a different character. The limb now showed soundly healed scars of operation and a number of firm, raised, bluish swellings, like thrombosed varicose veins. X-Ray examination did not demonstrate any phleboliths. The condition was very satisfactory and /

and the patient was able touse the limb for heavy labouring work. This case was, therefore, of outstanding interest, in being an example of a very extensive type of glomangioma, in marked contrast to the typical small localised lesion usually found. Whether arterial blood circulated in the veins of the lesion was a point which was not recorded.

In a survey of the literature on congenital arterio-venous fistula and on glomangioma, there has been little mention of the fact that an abnormality of the glomus could produce the effects of a pathological arterio-venous fistula. This fact is indeed surprising because the glomus is a normal variety of arterio-venous anastomosis and one might expect its derangements to give rise to pathological fistulae. Popoff (159) did not mention that point, but did enumerate the differences between the normal peripheral Sucquet-Hoyer anastomoses of the extremities and the digital arterio-venous anastomoses of the type of vascular anomaly. This case reported by me must surely be one of the first in which clinical examination proved the presence of arterio-venous fistulae and in which pathological examination revealed the features of a glomangioma.

In the present case, the presence of four lesions in different parts of the body was of interest, although only one had grown to a large size. It seemed that all four had arisen independently and there was no suggestion that one was a primary tumour and the others were secondary or metastatic. Each of the three small lesions had the appearance of a glomangioma, and only the absence of pain was atypical. It was possible that at any time one of them might begin to enlarge, though all seemed quite quiescent on examination. Most cases of glomangioma previously reported were solitary and multiple lesions were rare. However, Harvey, Dawson and Innes (147) in figures 29, 30 and 31, illustrated a case of multiple small glomangiomata beneath the skin, in which the lesion became apparent at eighteen months, after which continued outcropping took place. These lesions were chiefly painless and there was thus a considerable similarity tomy own case.

Another condition to be considered in the diagnosis was the rare one generally known as Rendu-Osler-Weber disease. This takes the form of multiple hereditary angiomata or telangiectases of the skin and mucous membrance, associated with recurring haemorrhages, especiallyfrom the nose. According to Parkes Weber (115) minute red spots or flecks are the typical feature, but theymay develop into raised bluish nodules like venous angiomata. Though these lesions are hereditary and developmental, they most commonly appear /

appear in middle life and are not found at birth. It seems certain that my own case was not an example of this condition, although the two are probably allied.

The ultimate prognosis, as in most vascular anomalies, is uncertain. It is possible that no further trouble will arise. On the other hand, any one of the three remaining lesions may become painful or begin to enlarge, or a local recurrence may take place at the site of the operation. However, if careful supervision of the patient were to be carried out, it should be easy to deal early with any complications which might arise.

To summarise, a report has been given of a case of four independent glomangiomata, one of which became enlarged and produced the clinical features of arterio-venous fistulae.

Fig. 49, Case 9. Swelling in region of right wrist, with prominent venous dilatation in centre, covered by thin skin.

Fig. 50, Case 9. X-Ray film - soft tissue outline of swelling at lower end of right radius.

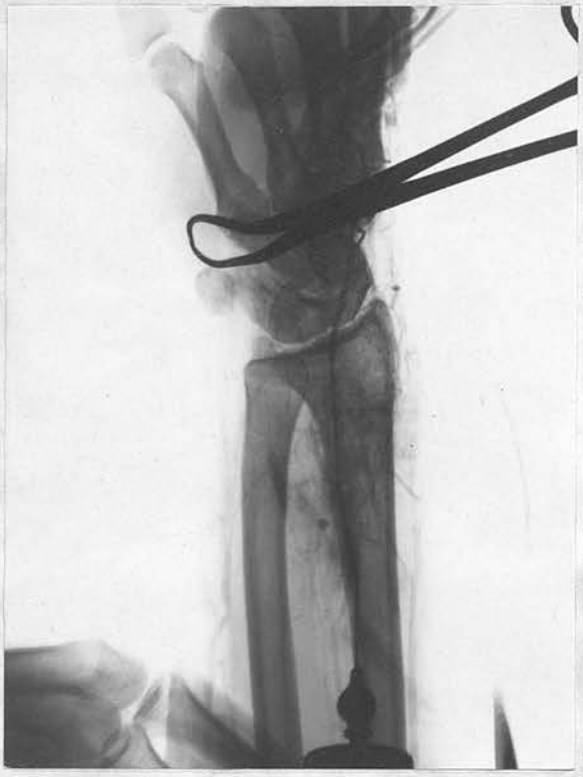


Fig. 51, Case 9. Arteriogram - opaque medium injected into radial artery and showing filling of artery, a plexus of vessels at site of lesion and main veins.

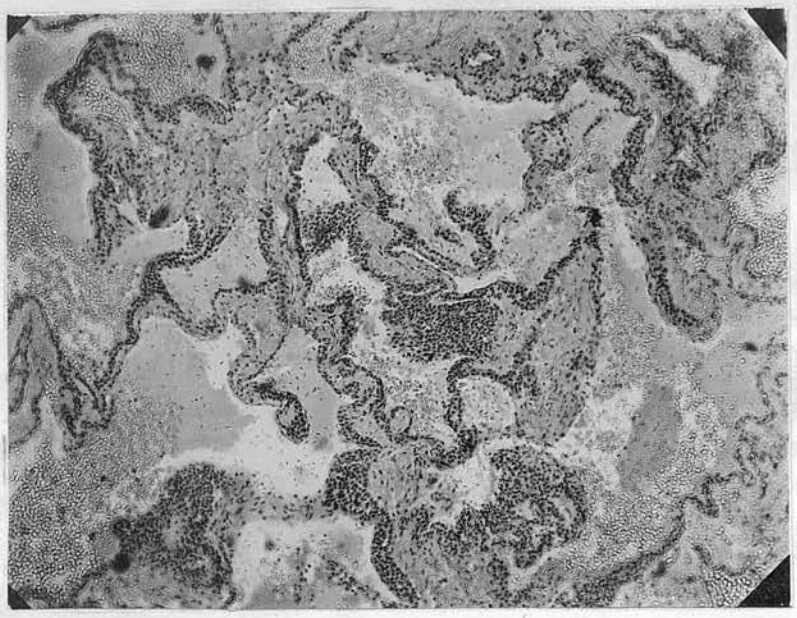


Fig. 52, Case 9. Microscopic section of glomangioma, LP, - irregular cavernous spaces, filled with blood.

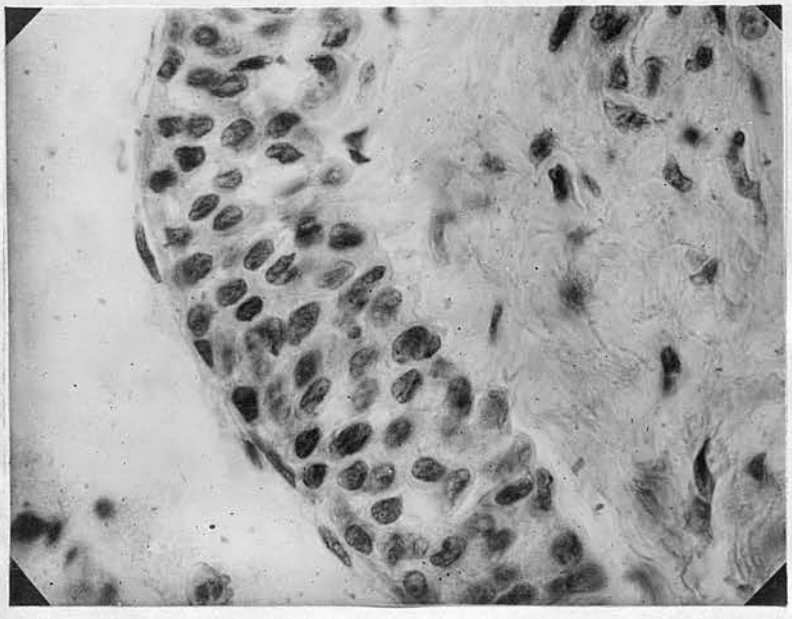


Fig. 53, Case 9. Microscopic section of glomangioma, HP, - single layer of flat endothelial cells lining spaces; typical glomus or epithelioid cells, four to five layers deep; fibrous tissue stroma.

CASE 10.

I.P. Female. Aged 14.

HISTORY.

Varicose veins of the left lower limb were noted shortly after birth. In the early years, the left foot and the left third finger were noted to have become larger than the opposites. Birthmarks were present in various situations. The patient was intelligent and well built, but there was a tendency to become easily fatigued. There was no disability nor any true disfigurement, and pain was absent.

CLINICAL FEATURES.

Varicose Veins.

Varicose veins of a severe degree were present in the left lower limb. The long saphenous vein was palpably enlarged in the upper half of the thigh and below that level it became visibly dilated and tortuous. In the calf and the dorsum of the foot the vein had many tortuous enlarged tributaries. The Trendelenburg test showed complete incompetence of the valves and a cough impulse was present. There was no pulsation in the veins.

Angiomata.

Several angiomata of the capillary type were present. On the dorsum of the left foot there was a large bluish red haemangioma, which was most pronounced with the limb dependent and became pale on elevation. Elsewhere in the lower limb there was a rather diffuse bluish blush, without any actual haemangioma. On the left upper limb there were multiple small mottled red haemangiomata, the most prominent being on the palmar surface of the hand. Three haemangiomata about one inch in diameter were present in the left supraclavicular region, the left scapular region and the left side of the back of the neck. A deep red haemangioma, about 3 inches X 1 inch in size, occupied the medial side of the right buttock and had very prominent veins coursing over it. A large haemangioma in the back was centred over the fifth lumbar vertebra and spread out equally on both sides. A smaller lesion was noted on the left lower abdominal wall but none was present on the face.

Hypertrophy in the Limbs.

Left lower limb. The two lower limbs were equal in the measurement between the anterior superior iliac /

iliac spine and the medial malleolus. There was no difference in circumference in the thighs and upper parts of legs, but below that level changes were apparent in both length and circumference. The following more important readings were recorded:-

Length.	Right.	Left.
Foot.	9¼ ins.	9¾ ins.
Toes - First.	2 "	2½ "
Second.	2 "	2¾ "
Third.	1¾ "	2 "

Circumference.	Right	Left - elevated.	Left - dependent.
Ankle.	9 ins.	10 ins.	10¼ ins.
Bases of metatarsals.	9 "	10 "	10 ½ "
Heads of metatarsals.	8½ "	9½ "	10 "
Toes - First.	2½ "	3 "	
Second.	2 "	2½ "	

Left upper limb. There was no generalised hypertrophy of the limb but changes were present in the fingers. The third finger was outstanding by its length. There had been a previous fracture of the left thumb, which was now stunted and was thus not comparable to the right thumb.

Length.	Right.	Left.
Fingers - Second.	3¼ ins.	3½ ins.
Third.	3½ "	4¼ "
Fourth.	3¼ "	3½ "
Fifth.	2⅜ "	2¾ "

Local Circulatory Effects.

In no situation was there any evidence of impairment of blood supply, such as ulceration or gangrene. The arteries were normal and there was no pulsation, thrill nor bruit in relation to the veins. An attempt was made to estimate the amount of blood lost into the veins of the lower part of the leg and foot on standing, the same technique being used as in Case One. In the left leg, the displacement of water was 210 c.c within one minute, indicating a considerable loss of blood from the general circulation.

General Cardio-Vascular Effects.

For several years this girl had shown an undue tendency to fatigue, such as having to retire to bed in the afternoon on coming home from school, becoming easily tired after walking and sometimes fainting. On examination /

examination of the heart, there was no abnormality in size, the heart sounds were normal and the rhythm regular. X-Ray examination showed no abnormality in the heart or lungs.

With the patient lying at rest, the pulse rate was 63 perminute, and the blood pressure, measured in an arm, was 120/80. On standing up, within a minute, the pulse rate rose sharply to 98 per minute, and the blood pressure altered to 115/90. These effects, as mentioned in Case One, were due to the sudden loss of blood into the large veins of the lower limb and illustrated a protective mechanism compensating for the impaired cardiac return.

SPECIAL EXAMINATIONS.

Oxygen Content of Venous Blood.

After the application of a tourniquet above the knee, specimens of blood were withdrawn from large superficial veins in the middle of the thigh and in the middle of the calf. Specimens were also obtained from veins in front of both elbows. The readings were as follows:- Left arm, 5.4 volumes %; Right arm, 5.1 volumes %; Left thigh, 5.6 volumes %; Left calf, 6.8 volumes %. At a later date, at the time of operation, a specimen was obtained from the saphenous vein, immediately below its entry into the femoral vein, and showed the normal colour of venous blood. Owing to unforeseen circumstances, a breakdown occurred in the technical apparatus for determining the oxygen content, and the specimen was thus wasted. The low readings obtained did not indicate any probability of the presence of arterio-venous fistulae.

Straight X-Ray Examination.

Straight X-Ray examination illustrated the variations in size of the feet, toes and fingers, but did not reveal any alteration in the structure of the bone.

Venography.

At the time of operation, after ligating and dividing the upper end of the long saphenous vein, a ureteric catheter was passed downwards and two injections of 10 c.cs of Pyelectan were made, thus allowing two exposures, for the upper and lower parts of the limb. The huge size, the multiplicity and the tortuosity of the veins were well shown. A similar investigation was made by injecting smaller quantities into a /

a vein on the front of the ankle, thus demonstrating the large veins in the foot. Arteriography was not carried out at the ankle in view of the very small size of the anterior tibial artery; there seemed little object in performing it at the femoral artery in view of the low oxygen content of the venous blood.

Skin Temperature Tests.

Accurate tests were not carried out, but the examining hand did not detect any difference in the temperature of the two lower limbs.

DIAGNOSIS.

A diagnosis was made of the congenital syndrome of varicose veins, angiomata and osteohypertrophy. No sign was present to indicate arterio-venous fistulae.

TREATMENT.

The only treatment considered necessary was that of the severe varicose veins, and accordingly, using a combination of twilight sleep and local anaesthesia, operation was performed. The long saphenous vein was exposed at its upper end, and was ligated flush with the femoral vein, after obtaining a specimen of blood from that site. Two inches of the vein were resected, and the distal end was ligated after venography had been carried out. The vein was also ligated and divided in two other places, in the lower third of the thigh and shortly below the knee. Finally, a large vein on the front of the ankle was ligated and divided after carrying out venography. In view of the possible sclerosing effects of the Pyelectan, no other sclerosing agent was injected into the veins. On completion of the operation, firm elastoplast bandages were applied from the toes to the groin. These were removed after three weeks and it was noted that the incisions above and below the knee were not completely healed and oozed spontaneously a small quantity of blood. This is a well known occurrence in such cases. The elastoplast bandages were repeated for three more weeks.

PATHOLOGICAL EXAMINATION.

At the time of operation a portion of vein was excised from the thigh, and histological examination showed a moderate but distinct increase in the amount of plain muscle tissue present in the media, indicating some degree of hypertrophy of the media.

SUBSEQUENT /

SUBSEQUENT COURSE.

Very satisfactory thrombosis took place in the whole length of the long saphenous vein and less swelling of the limb took place on dependency. The pulse rate now rose from 63 to 85 per minute on assuming the erect posture from recumbency, indicating that the amount of blood lost from the general circulation had been reduced, with consequent diminution of the cardiac effects.

COMMENT.

Most of the facts mentioned in the comment on Case One are applicable to this case, which appears to be a similar but less marked example of the same pathological condition. In this case, however, there was no indication of any arterio-venous communication, whereas in Case One this possibility existed in one lower limb.

Fig. 54, Case 10. Large size of first and second toes, left foot; varicosity on lateral side left ankle.

Fig. 55, Case 10. X-Ray film - large size of first and second toes left foot; no structural change in bones.

Fig. 56, Case 10. Varicose long saphenous vein left lower limb; discolouration of dorsum of left fore-foot due to haemangioma.

Fig. 57, Case 10. Venogram - visualisation of large venous plexus in leg after injection of opaque medium in thigh; veins in lower part of leg and foot not filled.

Fig. 58, Case 10. Large size of left third finger; patchy discolouration of forearm due to haemangiomata.

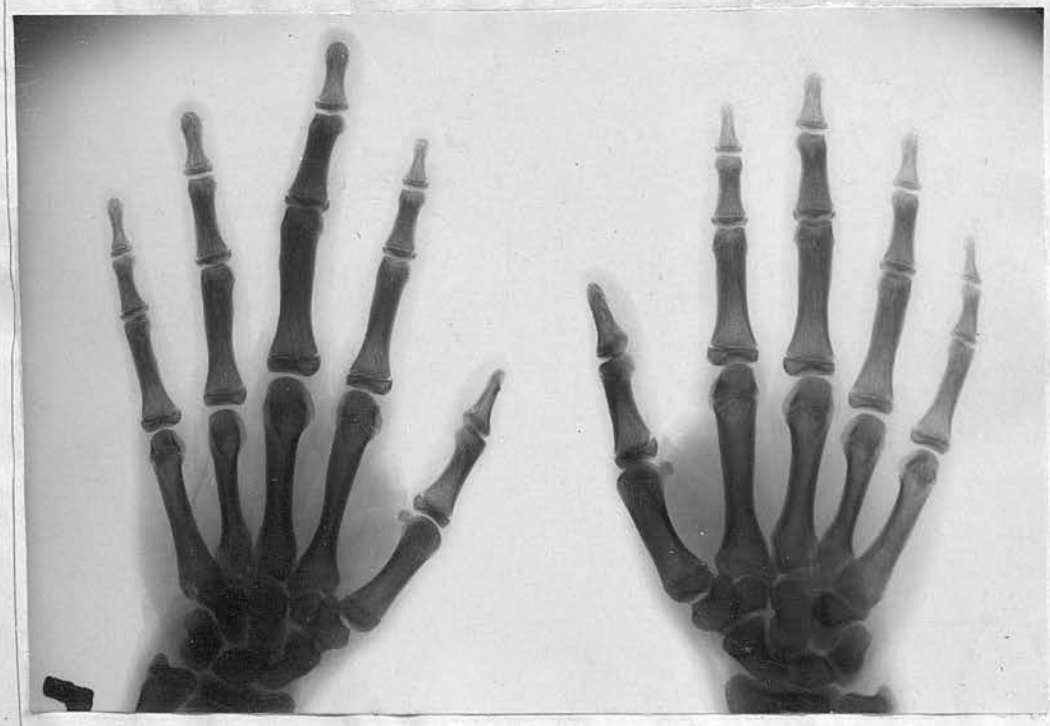


Fig. 59, Case 10. X-Ray film - large size of metacarpal and phalanges of left third finger.

Fig. 60, Case 10. Large haemangioma over lower lumbar region and smaller one in left scapular region near mid line.

CASE 11.

J.T. MALE. Aged 9.

HISTORY.

No abnormality was detected at birth, but at about the age of two a limp developed and an enlargement of the right lower limb became apparent. No birthmarks were noted and there was no history of pain. The boy seemed in good general health and was able to ride a bicycle, but he did suffer from fatigue after relatively slight exertion.

CLINICAL FEATURES.

Hypertrophy of the Right Lower Limb.

A gross degree of hypertrophy affected the entire right lower limb. On standing upright, the boy bore weight only on the toes of the normal left lower limb, and, on attempting to stand with both feet flat on the ground, a severe degree of lumbar scoliosis and lordosis developed. The buttock was large and the limb was enlarged in both length and circumference, the change being most striking in the leg. The following measurements were recorded:-

Length.	Right.	Left
Anterior superior iliac spine - medial malleolus.	27½ ins.	25 ins.
Tibia.	12½ "	10½ "
Foot.	8 "	7 "
Circumference.		
Mid thigh.	15 ins.	14 ins.
Mid calf.	11 "	9½ "
Base of metatarsals.	9 "	7½ "

Haemangiomata.

Three small bluish red patches, of a capillary nature and not more than ½ inch in diameter, were present on the dorsum of the foot and were more obvious on dependency.

Varicose Veins.

There was no outstanding degree of varicosity in the right lower limb. Several moderate sized superficial veins were present on the dorsum of the foot and in the neighbourhood of the knee, particularly over the popliteal /

popliteal space. Prominent veins also coursed over the buttock, between the greater trochanter and the iliac crest. The veins were not incompetent and the blood in the veins flowed upwards. No varicose veins were present in the left lower limb.

Local Circulatory Effects.

All the pulses in the right lower limb were stronger than in the left. There was a visible diffuse pulsation of the upper end of the right femoral artery, and, on auscultation, this pulsation was audible over the same area and also for three inches beyond. There was no actual bruit over the artery, and in no situation was there a pulsation, a thrill or a bruit in relation to the veins. There was no sign of any impairment of the distal circulation in the limb. On elevation of the limb, there was a decrease of $\frac{1}{2}$ inch in the diameter at the mid thigh.

General Cardio-Vascular Effects.

The boy showed a tendency to undue fatigue after exertion. The pulse, while usually of a normal rhythm, at times exhibited numerous extra systoles, and the apex beat was in the fourth left intercostal space in the mid-clavicular line. While at rest in the recumbent position the pulse rate was 80, but, on standing, it rose within a minute to 100 per minute. At rest the blood pressure measured in the arms was 120/80 and at the right medial malleolus 118/80; there was no significant change on assuming the erect posture.

SPECIAL EXAMINATIONS.

Oxygen Content of the Venous Blood.

Blood withdrawn from a prominent superficial vein behind the right knee was bright red in colour, and was found to have the high oxygen content of 16.3 volumes %, thus indicating the presence of arterial blood in the veins.

Blood Volume.

The blood volume was estimated by the Evans Blue Method and the readings obtained were:-

Blood volume = 2193 c.c.
= 74.8 c.c per Kg.
= 2120 c.c per sq. metre.

These figures were inconclusive as no comparable figures for children were available.

Straight /

Straight X-Ray Examination.

The two tibiae and the two femora were taken on the same films, the increased size of the one side being well shown. No pathological changes were present in these bones, in the pelvis or in the soft parts.

Arteriography.

This examination was carried out by Professor J.R. Learmonth after exposing the upper end of the femoral artery. 15 c.c of Perabrodil 50% were injected but no abnormality was detected in the lower part of the thigh and the leg.

Skin Temperature Test.

The entire right lower limb was obviously much hotter to the touch than the rest of the body, and the following accurate skin temperature readings were obtained:-

	Right	Left.
Side of buttock.	34°C.	29.5°C.
Thigh 10 c.ms above patella.	33.25	30.75
Medial side of calf.	30	28.5
Below medial malleolus.	30	26.25
Great toe.	24.5	20.75

Vaso-Motor Response to Body Heating.

Readings were obtained from the right great toe, the left great toe and the left third finger but no sign of vaso-motor paralysis was detected.

DIAGNOSIS.

A diagnosis of congenital arterio-venous fistulae was made, based on the clinical appearances and the high oxygen content of the venous blood. The fistulae almost certainly involved the common iliac vessels, and perhaps also those at a lower level.

TREATMENT.

The only treatment suggested at the present time was the wearing of a high boot on the normal lower limb. This allowed walking to be quite comfortable, without any awkward gait. At a later date, when fully grown, some operative procedure to equalise the length of the limbs was contemplated.

COMMENT.

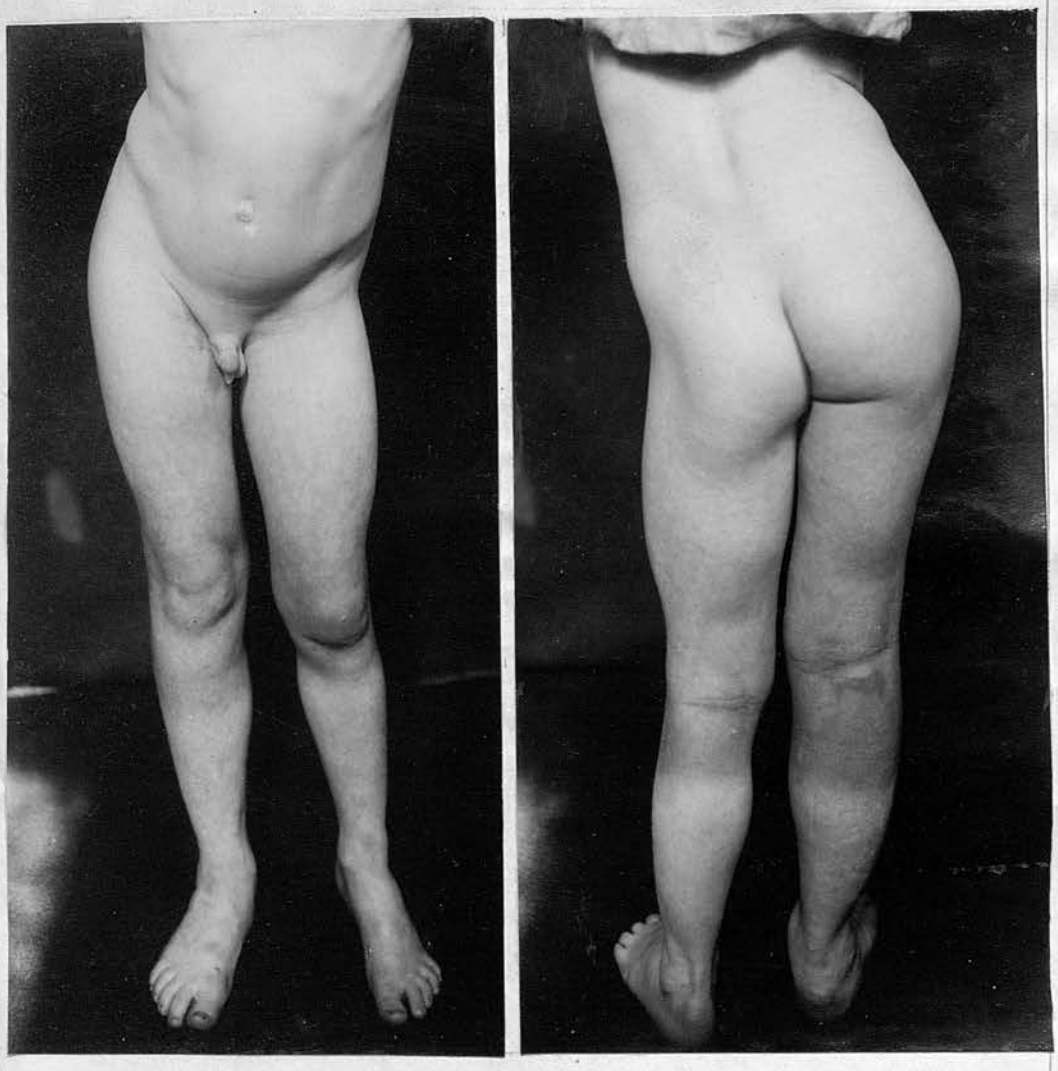
COMMENT.

This case demonstrated a gross enlargement of the whole of a lower limb, affecting bone and soft tissues alike, and the leg and foot showing a relatively greater increase in size than the thigh. Haemangioma formation was of small extent and the degree of dilatation of the superficial veins was moderate. The triad of hypertrophy, haemangiomata and varicose veins was thus certainly present, as in other cases, and in particular there was a strong resemblance to Cases Three and Four, except for the much less prominent haemangiomata. Such individual variations in the intensity of the three features are well recognised, however. In view of the fact that the hypertrophy implicated the entire limb, including the buttock, it was concluded that arterio-venous fistulae involved the iliac vessels. The arteriogram did not demonstrate any fistulae in the main vessels of the thigh or leg, but it was not possible definitely to exclude fistulae in the smaller vessels.

The diagnosis of arterio-venous fistulae was only made certain, however, by the high oxygen content of 16.3 volumes per cent in the blood of a superficial vein in the thigh, and once again the importance of the test was emphasised in the absence of more obvious signs such as venous pulsation, a thrill and a bruit. Other typical findings in vascular anomalies were the increased pulse rate on standing and the great increase in temperature of the limb. The estimation of the blood volume is more commonly carried out in traumatic than in congenital arterio-venous fistulae, but it is believed to have a doubtful significance. In the present case the results were inconclusive in the absence of comparable figures for children.

Points relating to prognosis and treatment and suitable references are mentioned in the Comments in Cases Three and Four.

To summarise, a report has been given of a case of arterio-venous fistulae of the iliac vessels.



Figs. 61 & 62, Case 11. Great increase in length and girth of entire right lower limb, including buttock; tilting of pelvis and scoliosis; varicose vein right popliteal region.

Fig. 63, Case 11. X-Ray film of both legs - great increase in length of right tibia and fibula.

CASE 12.

M.B. FEMALE. Aged 8.

HISTORY.

At birth it was noted that the right ear was discoloured and larger than the left, and during the ensuing years this difference in size became more pronounced. At no time was there any complaint of pain or discomfort, nor had haemorrhage or ulceration ever occurred. The general health was always good, except for a recent attack of pneumonia.

CLINICAL FEATURES.

There was a very striking and uniform enlargement of the right auricle, which was fully two and a half times the size of the other and was due to involvement of both the cartilaginous framework and the overlying soft tissues. Affecting the skin of the auricle, the retro-auricular skin, and the skin of the neck below the auricle almost as far as the clavicle, there was a pronounced deep bluish red discolouration with many prominent veins coursing through it. The veins exhibited strong pulsations, which had the effect of giving a vigorous expansile pulsation to the entire auricle. On palpation, the skin was easily compressed, soft and velvety, and there was a forcible thrill, more prominent during systole. Auscultation revealed the so-called machinery murmur, a loud continuous bruit, with considerable accentuation during systole, which could be heard over a wide area, but with the site of maximum intensity between the lobule of the ear and the mastoid process. As judged by the examining hand, the skin of the affected region was much hotter than that of any other part. No general cardio-vascular effects were demonstrated.

SPECIAL EXAMINATION.

The Blood Volume.

As estimated by the Evans Blue method, the blood volume was 2040 c.c, = 85 c.cs per Kgm, = 2270 c.cs per sq. metre. This reading was within normal limits.

DIAGNOSIS.

A diagnosis was made of an arterio-venous fistula involving the posterior auricular artery and vein.

OPERATION.

The /

The operation was performed by Professor J.R. Learmonth. A long incision was made along the anterior border of the right sterno-mastoid muscle, the external jugular vein being divided between ligatures and the great auricular nerve being sacrificed. The external carotid artery was identified, and, distal to the origin of the lingual artery, a temporary ligature was placed round it, traction on which abolished the pulsations and the bruit, as tested with a sterile stethoscope. The dissection was continued upwards and the digastric muscle was divided close to its tendon, the posterior belly then being turned backwards, thus exposing the posterior auricular artery, which was divided between ligatures. The skin incision was extended, curving below and behind the auricle, in order to expose the insertion of sterno-mastoid, which was then detached and turned backwards. Many vessels communicating with the auricle were thus exposed and were treated either by ligature or electro coagulation. The external carotid artery was finally divided between ligatures at the point of its temporary occlusion, the digastric muscle was reconstituted and the wound was closed.

A dramatic improvement was evident at the conclusion of the operation. The auricle was considerably reduced in size, the intensity of the colour of the auricle and surrounding skin was much diminished, the enlarged veins were no longer prominent and the abnormal pulsations, the thrill and the bruit were absent. It was now evident that the large size of the auricle had been due both to an enlargement of the cartilage, which was not affected by the operation, and to a vascular engorgement and oedema of the soft tissues.

SUBSEQUENT PROGRESS.

The wound healed quickly and the patient was discharged from hospital a fortnight after the operation. On examination three months later, the excellent result had been maintained. In was considered probable that, in the near future, a plastic operation would be carried out on the auricle in order to reduce its size still more by excising a portion of its cartilaginous framework.

COMMENT.

This case was an excellent example of an arterio-venous fistula of the posterior auricular vessels, and, on account ofthe intensity of the pulsations, the thrill and the bruit, it was believed that the communication was single and large, instead of multiple and small as in most congenital cases. The large cutaneous haemangioma, the extensive pulsating veins /

veins and the large size of the auricle thus constituted the triad seen more often in the limbs. In former years, a diagnosis such as pulsating angioma, cirsoid aneurysm or aneurysm by anastomoses would probably have been made, the impression being conveyed that the lesion was a tumour. Although no pathological examination was made, the findings during operation definitely confirmed the presence of a vascular anomaly.

The operation did not expose the deeply placed fistulous track between the posterior auricular artery and vein, but it was in the nature of a quadruple ligation, allied to that so successful in traumatic lesions. The artery was ligated both proximal to the fistula in the neck, and distal to it overlying the mastoid process. The ligation of the external jugular vein inferred an interruption of the proximal flow of blood from the posterior auricular vein, and the ligation and coagulation of the retro-auricular veins constituted the distal obliteration of the vein. The result of the operation was extremely satisfactory and the risks of recurrence must be remote. One potential hazard, however, lies in the fact that, in the segment between the two ligations, the stylo-mastoid branch leaves the posterior auricular artery and eventually anastomoses, chiefly with the petrous branch of the middle meningeal artery and the tympanic branch of the maxillary artery. Thus it is possible that blood might ultimately find its way through these anastomoses into the fistula, and thereafter it could pass into the venous system by way of the posterior division of the posterior facial vein. The additional step at operation of ligating the external carotid artery should do much to avoid this happening.

Among my personal cases, Case Six afforded an interesting comparison, as here also branches of the external carotid artery and tributaries of the jugular veins were implicated. Instead of a single large fistula, however, there must have existed numerous small communications, sufficient to cause a high oxygen content of the venous blood but not large enough to induce pulsations, a thrill or a bruit. Case Five, although involving the foot, exhibited a similarity on account of the fairly well localised, pulsatile lesion.

Reference to the literature shows that similar cases involving the auricle have been reported by Mussey in 1853 quoted by Elkin (21), Eve in 1880 and Brandau in 1892, both quoted by Rienhoff (22), Duncan (10), Dean Lewis (41), the veins here perforating the auricle, and Luke (108).

In contrast to the hypertrophy of bone found in several of my cases, in the present instance the hypertrophy involved the cartilaginous framework of the auricle. Bone is a richly vascular tissue and several vascular /

vascular influences have been credited as responsible for the increase in its growth. Cartilage, on the other hand, is an avascular tissue, believed to derive its nutrition from lymph, and criticism can be levelled justifiably against the tendency to ascribe the occurrence of hypertrophy of cartilage to the increased amount of blood passing along the arteries. The cause of the hypertrophy of the cartilage of the auricle is thus by no means certain, but the subject will be discussed more fully in Section Eight.

To summarise, a report has been given of a case of an arterio-venous fistula of the posterior auricular vessels.

Fig. 64, Case 12. Large size of right auricle; large haemangioma causing pigmentation of skin of auricle and skin behind it; prominent dilated veins.

Fig. 65, Case 12. Tracing of previous illustration, to show large size and extent of dilated veins.

S E C T I O N T H R E E.

A PRESENTATION OF CASES OF CONGENITAL VASCULAR ANOMALIES PREVIOUSLY REPORTED IN THE LITERATURE.

BUSHE (1) 1827. F.2. Pulsating, anastomosing aneurysm R. temple, associated with repeated haemorrhages and ulceration. It was removed by " a few quickly executed sweeps of a scalpel". Severe haemorrhage at operation and also later, necessitating ligation of external carotid artery. Cure.

MOTT 1829 quoted by Rienhoff (22). No details, but probably congenital arterio-venous aneurysm.

MUSSEY 1829 quoted by Rienhoff (22). Pulsating tumour of the vertex of the head - probably congenital arterio-venous aneurysm.

LISTON 1843 quoted by Davis (13a). Pulsating, congenital angioma in Semimembranosus. Excision and recovery.

NORRIS 1843 quoted by Rienhoff (22). No details, but probably congenital arterio-venous aneurysm.

WARREN 1846 quoted by Rienhoff (22). Pulsating tumour of forehead - probably congenital arterio-venous aneurysm.

LAUGIER 1851 quoted by Callander (114). Arterio-venous aneurysm posterior auricular vessels.

MUSSEY 1853 quoted by Elkin (21). Cirsoid aneurysm of ear.

GIRALDES 1854 quoted by Reid (76). Cirsoid aneurysm lower limb. (Not definitely congenital).

BROCA 1856 quoted by Pearse and Morton (145); Finlayson (7); Tavernier (85). M. 17. Arterio-venous aneurysm of lower limb, with hypertrophy.

DEVOUGES 1856 quoted by Finlayson (7); Klippel and Trenaunay (11); Lee W.E. and Freeman (89). Extensive angiomata, varicose veins, and hypertrophy of a lower limb. Also angiomata and hypertrophy of first three fingers of hand of same side.

WARREN 1858 quoted by Ward and Horton (98). Varicose aneurysm of arm, with arterial blood in veins.

ADAMS /

ADAMS, J. (2) 1858. Two cases of congenital arterio-venous fistula.

(1) M. 19. Hypertrophy and dilated arteries and veins R. lower limb; large naevus stretching from lower lumbar vertebrae to toes, and involving half of scrotum.

(2) Enormous hypertrophy of arteries and veins of a lower limb. This involved the calcaneus, from which a fatal haemorrhage ultimately took place.

CHASSAIGNAC 1858 quoted by Finlayson (7); Klippel and Trenaunay (11). Male. Hypertrophy of R. upper and lower limbs; multiple naevi, varicose veins and trophic disorders of soft parts.

CHASSAIGNAC 1859 quoted by Finlayson (7). Female. Hypertrophy and naevus one limb.

LETENNEUR 1859 quoted by Weber (116); Lewis, D. (41). M. 43. Arterio-venous aneurysm forearm and hand. Amputation carried out for haemorrhage.

CHERRY 1859 quoted by Rienhoff (22). No details, but probably congenital arterio-venous aneurysm.

PEMBERTON, O. (3) 1860. F. 15. Large pulsating tumour of upper lip, probably congenital arterio-venous anastomosis; contained arterial blood.

WARREN 1861 quoted by Rienhoff (22). (May be same case as reported for 1867 by Elkin). Cirsoid aneurysm of forehead.

KRAUSE 1861 quoted by Weber (116); Lewis D. (41); Pearse and Morton (145). M. 33. Arterio-venous aneurysm forearm and hand. Eventual amputation.

POLAND 1865 quoted by Colley R.D. (88). F. 19. Cirsoid aneurysm of foot, producing a pulsatile swelling. Eventual amputation. Dissection showed masses of cavernous tissue communicating freely with arteries and veins.

PASSAUER 1866 quoted by Finlayson (7). Vascular hyperplasia of face and tongue.

FRIEDBERG 1867 quoted by Finlayson (7). F. 10. Dilated veins and congenital gigantism R. lower limb, producing scoliosis. Also congenital elephantiasis des Arabes L. arm (i.e. probably due to a lesion involving the lymphatics).

HEWETT /

HEWETT (4) 1867. F. 17. Hypertrophy of lower limb. Superficial veins of limb dilated and compressible, with thrill and bruit. Treated by underrunning veins with hare lip pins, but without much improvement. Believed to be an arterio-venous fistula between R. common iliac artery and vein.

GROSS 1867 quoted by Lewis, D. (41); Callander (114); Rienhoff (22). F. 43. Hypertrophy of leg and foot; naevus of foot; dilated pulsating vessels and ulceration. Eventual amputation. Dissection showed numerous arterio-venous fistulae, including the vessels of the tibia and fibula.

GHERINI 1867 quoted by Lewis, D. (41) and Rienhoff (22). F. 9. Arterio-venous fistulae forearm and hand. Hand warmer than opposite hand or rest of body. Brachial artery enlarged and tortuous; dilated veins with pulsation and bruit. Ligation of radial and ulnar arteries gave improvement but no cure.

LEE, H. (5) 1867. Two cases.

(1) M. 59. Arterio-venous fistulae over L. rectus abdominis with thrill and bruit; also varicose veins both lower limbs.

(2) Museum specimen. Enormous dilatation of veins of arm invading biceps brachii but with no obvious connection between arteries and veins.

VON PATHA 1869 quoted by Freund (56). Phlebectasis of upper limb.

TRELAT and MONOD 1869 quoted by Finlayson (7); Klippel and Trenaunay (11); Telford (16); Lee, W.E. and Freeman (89). Angiomata, varicose veins and osteo-hypertrophy of lower limb.

MONOD 1869 quoted by Klippel and Trenaunay (11). Male. Hypertrophy of R. upper and lower limbs and side of trunk; scattered naevi stopping abruptly at mid line; varicose ulcer of leg.

OBALINSKI and BROWICZ 1874 quoted by Weber (116); Lewis, D. (41). F. 30. Vascular tumour of forearm and hand, regarded as a racemose angioma. Bleeding and gangrene necessitated amputation.

NICOLADONI 1875 quoted by Weber (116); Lewis, D. (41); Holman (61). M. 17. Vascular tumour (due to arterio-venous fistulae) on hand and finger at birth, which increased and finally reached supraclavicular region; dilated vessels; limb longer and thicker than /

than opposite limb. Cardiac changes and bradycardia re-action noted for first time.

NICOLADONI 1876 quoted by Weber (116); Lewis, D. (41) M. 22. Vascular tumour (due to arterio-venous fistulae) of hand and fingers; ulceration; limb longer and thicker.

ISRAEL 1877 quoted by Lewis, D. (41); Pearse and Morton (145); Holman (61). F. 9. Arterio-venous fistulae of R. lower limb with hypertrophy and ulceration of leg. Bradycardia test showed a reduction in pulse rate of 42beats per minute. Prominent veins, pulsation, thrill and bruit. Proximal ligation of femoral artery followed 5 weeks later by amputation through thigh. Specimen showed arteries entered large blood spaces which communicated directly with veins.

DESPRES 1879 quoted by Rienhoff (22). Arterio-venous fistulae of tongue and neck, giving rise to a thrill and a pulsatile swelling below jaw.

WITTELSHOFER 1879 quoted by Finlayson (7). Recorded 46 cases of unilateral hypertrophy and vascular abnormality.

EVE 1880 quoted by Rienhoff (22). Congenital aneurysmal tumour of ear.

PETIT, L.H. 1880 quoted by Weber (116). Several examples of congenital varicose veins of arm.

SMITH, SIR T. (6) 1882. F. 25. Angiectasis of hand and fingers. Hand larger and temperature higher. Arteries and veins enlarged and tortuous; bruit and thrill. Communications believed to be present between arteries and veins by greatly dilated capillaries.

DOMAINVILLE 1883 quoted by Rienhoff (22). F. 43. Naevus on cheek at birth, which became large pulsating tumour. Treated by electrolysis and later by ligation of common carotid artery.

FINLAYSON (7) 1884. F. 1½. Lesion noted at birth. Hypertrophy of R. side of body from head to toes, and also hypertrophy of three middle fingers L. hand. Widespread angiomata. Temperature of R. side of body greater than of L. side. Eight teeth present on R. side before any on L. side.

AUDRY 1885 quoted by Klippell and Trenaunay (11). Naevi and hypertrophy L. index.

MONDAN 1885 quoted by Klippel and Trenaunay (11). Naevi and hypertrophy L. fourth metatarsal and fourth toe.

DUZEA /

DUZEA 1885 quoted by Klippel and Trenaunay (11). Six cases:-

(1) M. 34. Large angioma of entire R. lower limb, with hypertrophy and varicose veins.
(2) M. 65. Angioma and hypertrophy R. lower limb.
(3) F. 14. Angioma and hypertrophy L. leg.
(4) - Angioma and hypertrophy L. forearm.
(5) M. 28. Angioma of R. side of face, neck and chest with hypertrophy of jaws of R. side.
(6) M. 30. Angioma L. half of skull and hypertrophy.

TREVES (191) 1886. M. 17. Pulsating tumour of head.

BARWELL 1875 quoted by Finlayson (7). Vascular hypertrophy of lower part of face.

BARWELL 1881 quoted by Klippel and Trenaunay (11). Angioma of R. ear and hypertrophy of R. side of face.

BARWELL 1887 quoted by Bland-Sutton (17) and similar to case reported by him. Condition given the name of macroangiosis.

MASMÉJEAN 1888 quoted by Klippel and Trenaunay (11). Hypertrophy of half of the body, associated with naevi. (No definite case quoted).

PALMGREN 1889 quoted by Freund (56). Two cases. F. 14 and F. 26. Phlebectasis of upper limb.

MÜLLER and BRÜNS 1891 quoted by Bland-Sutton (127); Elkin (21). A classical case with well-known illustration. Started as red spot on forehead at 1 year in a male child and increased in size. At age 20 gave all characteristics of a plexiform angioma, with pulsation and buzzing, and occupied large area of scalp. Ligation of R. external carotid and L. common and external carotid arteries was followed by hemiplegia and death. Several arteries led into the mass of vessels of which the angioma was composed.

MEYER 1892 quoted by Elkin (21). Arterio-venous fistulae of temple.

BRANDAU 1892 quoted by Rienhoff (22). M. 15. Naevus present at birth, which grew to become a pulsating arterial tumour of ear and scalp. Due to arterio-venous fistulae.

LITTLE (8) 1893. F. 15. At birth diffuse naevus over almost all R. side of body; large tortuous veins; upper limb 1½ inches longer and increased in circumference; lower limb 2 inches longer.

ABBE /

ABBE 1894 quoted by Gould and Pyle (123a). M. 9. Arterio-venous aneurysm of hand.

FORBES 1895 quoted by Elkin (21). Cirsoid aneurysm of scalp.

BEAUMONT (9) 1897. F. 22. Cirsoid aneurysm of scalp, composed of a plexiform mass of vessels fed by many arteries, and covered by dusky skin. Treated by ligation of feeding vessels and passage of electric current through transfixion needles.

LEBLANC 1897 quoted by Klippel and Trenaunay (11); Telford (16). Described 80 cases of bony hypertrophy, angiomata and varicosities.

DUPLAY 1898 quoted by Klippel and Trenaunay (11); Telford (16). Hypertrophy, naevi, varicose veins and ulceration of L. leg.

VON EISELBERG 1899 quoted by Lewis, D. (41); Rienhoff (22). F. 26. R. leg larger, with ulceration and pain. Ligation of femoral artery followed by amputation. Specimen showed a large varix between popliteal vessels.

VON SCHROTTER 1899 quoted by Lewis, D. (41). Male. Arterio-venous fistulae L. upper limb. All arteries and veins dilated, thick and tortuous. Pulsatile, elastic swelling of hypothenar eminence, and also pulsation and bruit over whole limb. Improvement after ligation of ulnar artery. At later date to have radial artery ligated and veins excised.

DUNCAN (10) 1900. Ten cases included under title of angioma:-
(1) M. 27. Tortuous dilated veins of arm and neck; several phleboliths.
(2) Child. Naevus of foot, involving fourth metatarsal. Cured by electrolysis.
(3) Child of 6 months. Naevus upper limb and cheek. Cured by electrolysis.
(4) M. 19. Pulsating angioma of L. cheek. Cured by electrolysis.
(5) M. 47. Pulsating angioma of buttock and thigh.
(6) M. 42. Aneurysm by anastomosis of R. shoulder and neck. Strong pulsation and loud systolic bruit, indicating close communication between arteries and veins.
(7) Female. Pulsating cavernous tumour of submaxillary region. Not improved by electrolysis.
(8) Cirsoid aneurysm of palm of hand.
(9) M. 25. Pulsating cirsoid aneurysm of posterior auricular artery. Cured by electrolysis.
(10) F. 18. Pulsating cirsoid aneurysm of scalp. Improved with electrolysis.

BAJARDI 1900 quoted by Davis (13a) F. 12. Arterial and cavernous angioma of flexor digitorum longus. Tibial artery and nerve involved in tumour.

KLIPPEL and TRENAUNAY (11) 1900. "Naevus variqueux osteo hypertrophique" of lower limb. Hypertrophy, extensive naevus, and abundant varicosities.

BRAUN 1901 quoted by Weber (116); Lewis, D. (41). M. 43. Phlebarteriectasis or cirsoid aneurysm of R. upper limb. Believed to be purely a dilatation of the vessels, without any actual new formation of blood vessels.

COLEY 1901 quoted by Elkin (21). Cirsoid aneurysm of temple.

GRIMAUD 1901 quoted by Telford (16). No details but case similar to that reported by Telford.

ROXBURGH 1902 quoted by Weber (116) F. 5. Hypertrophy, angioma and varicose veins lower limb.

HAWTHORNE 1902 quoted by Weber (116). M. 10. H ypertrophy, angiomata, varicose veins and dilated arteries lower limb.

SCENDRO 1903 quoted by Davis. (13a) Pulsatile cavernous angioma of temple with phleboliths.

NAGATOMI 1905 quoted by Davis. (13a) Pulsatile diffuse cavernous angioma of gluteal muscles. Excision.

PUTTI 1906 quoted by Davis (13a). F. 29. Cavernous angioma and varicose veins of lower limb. Excision.

BERRY (12) 1906. F. 39. Large arterio-venous aneurysm of R. side of neck, forming pulsatile tumour with loud murmur and thrill. At operation, several arteries, including external carotid, and many veins were ligated and a mass of tortuous, distended veins was removed. The fistula was near the origin of the external carotid artery. He believed that in cirsoid aneurysm, as in this case, the tumour mass consists of dilated veins, not arteries as previously accepted.

BALLANCE, Sir C.A. (177) 1906. Two cases of doubtful congenital origin - one a cirsoid aneurysm of the scalp and the other a cirsoid aneurysm of the dorsum of the foot.

HEIDE 1906 quoted by Davis (13a); Freund (56). M. 12. Classified by the former as angioma of muscle and by the latter as phlebectasis. L. lower limb thickened but not longer; muscles and bones very atrophic /

atrophic; angiomata of this limb and also of L. upper limb; phleboliths.

KOLACZEK 1907 quoted by David (13a). F. 23. Hypertrophy, phleboliths and cavernous angioma of lower limb.

BOCKENHEIMER 1907 quoted by Weber (116); Freund (56). M. 52. Phlebectasis and hypertrophy of upper limb; ascending pulse in the enlarged veins and bruit. Amputation followed by death from sepsis.

DAVIS (13a) 1908. F. 12. Diffuse venous angioma leg and foot; varicose veins; hypertrophy.

FURLKROGER 1908 quoted by Davis (13a). M. 23. Diffuse cavernous angioma of short muscles of sole of foot. Amputation.

CLAIRMONT 1908 quoted by Elkin (21). Cirsoid aneurysm of scalp.

JORGE 1908 quoted by Davis (13a). M. 10. Cavernous angioma of forearm.

NAST-KOLB 1908 quoted by Davis (13a). F. 12. Diffuse cavernous angioma of all muscles of leg and foot; nerve involvement. Amputation.

KEPLER and HEINEKE 1910 quoted by Elkin (21). Cirsoid aneurysm of scalp.

MARCHETTI 1910 quoted by Davis and Kitlowski (13b). F.13. Cavernous angioma of muscles of upper limb; blue discoloration of skin; phleboliths. Amputation.

DENT (14) 1911. Child aged 4 months. Elephantiasis of upper limb, with haemangioma, lymphangioma and dilated veins.

FITZWILLIAMS (179) 1911. Extensive naevus lower limb; increase in size of limb. Femoral artery ligated.

BIRCHER 1912 quoted by Freund (56). M. 21. Phlebectasis of upper limb; phleboliths.

TELFORD (16) 1912. F. 7. Hypertrophy of entire R. side of body; extensive superficial angiomata of R. side; varicose veins of R. lower limb.

BALLIN 1913 quoted by Lewis D. (41). M. 30. Arterio-venous fistula of hand. A dilated arterial sac in the hand communicated with a large cavernous mass of veins. Eventual amputation.

LEREBOULLET and PETIT, L. 1914 quoted by Weber (116). M. 52. Varicose veins L. upper limb with progressive swelling of limb; fragility of bone causing ununited fracture of forearm.

PUSCH 1914 quoted by Lewis, D. (41). M. 12. Arterio-venous fistulae R. upper limb. Hypertrophy, increased temperature, dilated vessels, bruit and ulceration of fingers. Enlarged heart and relative aortic insufficiency.

JUDD 1916 quoted by Elkin (21). Cirsoid aneurysm of scalp.

BLAND-SUTTON (17) 1918. M. 25. Arterio-venous fistulae hand and upper limb. Arteries and superficial veins enormous. Veins pulsated like arteries, with a thrill and buzzing, and contained blood of same colour as that in arteries. Large blue compressible swelling of hand, diagnosed as cavernous angioma. Gangrene developed and amputation carried out. Specimen showed that superficial palmar arch sent branches to feed this angioma.

NOORDENBOS 1918 quoted by Elkin (21). Cirsoid aneurysm of forehead.

EBSTEIN quoted by Weber (116); Lewis, D. (41). Three cases of phlebarteriectasis or arterio-venous fistula.

(1) 1913. M. 24. L. upper limb hypertrophied; enlarged veins with thrill and bruit.
(2) 1917. Aged 14. R. forearm hypertrophied.
(3) 1918. M. 49. L. upper limb hypertrophied; enlarged veins with thrill and bruit; increased temperature.

ARMOUR (18) 1919. F. 58. Cirsoid aneurysm R. hand.

DRESSLER 1921 quoted by Freund (56). M. 15. Phlebectasis and angioma of L. lower limb and lower L. part of trunk; phleboliths. Limb shorter than opposite limb.

WAKELEY(19) 1921. F. 24. Slight hypertrophy R. leg; cavernous angiomas leg and ankle; phleboliths; wide venous sinuses.

MELENEY (20) 1923. M. 31. Cirsoid aneurysm of neck. Removed at operation after ligating lingual artery and other vessels. Specimen showed fairly large vessels communicating through a network; proliferation of endothelium, in arteries as well as in veins.

ELKIN /

ELKIN (21) 1924. M. 22. Cirsoid aneurysm of scalp. Treated by ligation of both external carotid arteries, reflection of scalp and puckering of swelling by multiple sutures.

RIENHOFF (22) 1924. M. 24. Arterio-venous fistulae between external carotid artery and external jugular vein. Pulsating rumbling mass L. side of neck since age of 3 weeks. Greatly distended veins with a palpable thrill and visible arterial pulsation in them. Pressure on common carotid artery stopped pulsation, and also produced dizziness and a definite bradycardia re-action, the pulse rate falling 20-30 beats per minute. L. retina more vascular. At operation external jugular vein very large, internal carotid artery very small and external carotid artery very much dilated. Eight fistulous communications dissected out between external carotid artery and external jugular vein, resulting in cure. Previously short winded but not so much now.

McFARLAND (23) 1924. F. 14. Cavernous haemangioma R. upper limb. Whole limb was a mass of angiomatous nodules and was spongy and soft so that blood expressed quickly returned.

STEWART and BETTIN (24) 1924. Six cases of angioma:-

(1) M. 26. Large cavernous angioma, starting at birth and eventually involving L. breast, neck, back and upper limb.
(2) F. 17. Dilated veins L. leg since age 2 months. Destruction of all parts of foot except skin and bones. Vascular disturbance of leg.
(3) F. 10. R. upper limb shorter but slight enlargement of arm; pectoral region bluish; entire limb livid with oedema of hand and fingers.
(4) M. 65. Large pulsatile vessels and varicosities of hand; tissues compressible; skin thin, with blue discoloration; ulceration. Injection and excision of mass of vessels.
(5) F. adult. Tortuous mass of veins in elbow region.
(6) M. 10. Large angioma R. leg since infancy, involving muscles and medial and lateral popliteal nerves. Limb shorter but of increased diameter. Eventual amputation.

BERNHEIM (25) 1925. M. 47. Arterio-venous fistula L. upper limb. Started as small red spot on wrist. Limb twice normal size, bluish red and encompassed by pulsating tortuous veins; intense bruit and thrill. Hand almost useless. X-Ray examination showed many phleboliths, absorption of head of radius and atrophy/

atrophy of bones of wrist and hand. At operation, double quadruple ligation of axillary vessels. Thereafter veins became very tense due to additional unsuspected arterial supply of blood entering them. Five days later amputation carried out below shoulder; terrific haemorrhage from huge blood sinuses in soft tissues and in bones. Recovery.

PATERSON and WYLIE (26) 1925. M.7. Hypertrophy of femur and tibia; angiomata and phlebectasis of R. lower limb; increased temperature.

VAN NECK 1925 quoted by Lee, W.E. and Freeman (89). Osteohypertrophy, varicose veins and cutaneous naevus of lower limb.

BELL and INGLIS (27) 1925-26. F. 17. Angioma of R. leg. Limb smaller but later became increased in size; increased temperature; pigmented areas; hard swelling of leg producing deformity of knee and ankle. Amputation. Specimen showed abnormal blood vessels which merged insensibly into angioma, causing replacement of muscle; posterior tibial artery absent. Microscopically, tissue made up of blood spaces.

BEATTY (28) 1926. F. 13. Cirsoid aneurysm of R. upper limb. Hypertrophy; large distended veins; angiomata; increased temperature. Soft tissue of forearm pulsatile.

SCHMIDT 1926 quoted by Freund (56). M. 17. Hypertrophy and phlebectasis upper limb; slender bones; phleboliths.

OREL 1926 quoted by Freund (56). M.6. Venectasia of lower limb, also affecting penis.

ERDHEIM 1926 quoted by Lewis, D. (41). M. 32. Phlebectasis of upper limb. R. forearm larger as a child; dilated vessels; blue compressible angioma of hand; later pulsation and bruit. Varices of aesophagus found on post mortem examination.

PERTHES 1927 quoted by Lewis, D. (41); Holman (61). F. 27. Arterio-venous fistulae L. lower limb. L. foot larger and entire leg swollen; dark spots on foot; bleeding ulcers; pain; bruit; superficial veins full of bright arterial blood. At operation femoral artery resected, followed later by amputation. Specimen showed that arterial blood passed through sieve-like congenital angioma and entered veins.

HARBIN (29) 1927. F. 12. Hypertrophy, angiomata and large veins of lower limb.

SUSMAN /

SUSMAN and McCREDIE (30) 1927. F. 15. Hypertrophy of upper limb, in circumference only; gross venous dilatation; bluish discoloration of hand and wrist.

GRAY (31) 1927, also reported by HARRIS, K.E. and WRIGHT, G.P. (32) in 1930. Haemangiectatic hypertrophy of R. lower limb, almost certainly due to arterio-venous fistulae. Large pulsating vessels, with thrill and bruit; capillary naevus and telangiectases; increased temperature; pigmented patch and ulceration of leg; bradycardia test present.

ROSLER 1928 quoted by Lewis, D. (41). M. 15. Arterio-venous fistula R. upper limb. Hypertrophy; prominent veins with pulsations, thrill and bruit; elastic swelling in hand.

PAUTRIER and ULLMO (33) 1928. M. 17. Hypertrophy, angioma and varicose veins R. lower limb.

REICHEL 1928 quoted by Freund (56). F. 14. Venectasia of lower limb. Also deformities of knee and foot. Muscle and sciatic nerve involved.

SONNTAG 1918 quoted by Freund (56). M. 17. Hypertrophy, angiomata and phlebectasis of lower limb; also phleboliths.

SONNTAG 1919 quoted by Lewis, D. (41).F. 16. Arterio-venous fistula of R. upper limb. Hypertrophy; bluish discoloration; increased pigmentation; increased temperature; ulceration of hand. Several resections of arteries and veins carried out.

SONNTAG 1928 quoted by Freund (56). Aged 22. Phlebectasis of R. upper limb. Increased size, but slight shortening; phleboliths; atrophy of muscles. Veins ligated.

LYLE (34) 1928. F. 20. Mass of varices of chest wall, found at operation to communicate with deeper arteries and veins.

PEMBERTON J. and SAINT (35). 1928. Seven cases of arterio-venous fistula.

(1) F. 23. A bunch of blue dilated veins of R. occipital and temporal regions at birth. Later became a large mass of pulsating veins, with loud bruit and thrill. Cardiac systolic murmur. At first operation, arterio-venous anastomosis found; external jugular vein very large; external carotid artery ligated and bunch of veins excised from neck. At second operation, 8 days later, cirsoid vessels /

vessels dissected from scalp. Death from broncho-pneumonia two and a half months later.

(2) F. 10. R. exophthalmos and bunch of dilated veins around eye, with thrill and bruit. External carotid artery ligated with success.

(3) See beyond.

(4) M. 21. Hard lump on head which bled furiously after ill-timed incision and later spread. Pulsating, tortuous mass of vessels in L. side of scalp, with thrill and bruit. At operation, area encircled with stitch and veins excised. Not definitely proved to be congenital.

(5) M. 30. R. upper limb larger; progressive abnormality; large veins of hand with thrill and bruit; even slight abrasion took two months to heal. Several operations:- arterio-venous aneurysm of ulnar artery and vein excised; radial artery communicated with large vein and both ligated; amputation of fifth finger; amputation of second and third fingers for gangrene. Later recurrence in hand; increased temperature of limb; oxygen saturation of blood from veins 99%; heart enlarged. Amputation carried out through forearm; veins bled like arteries. Dissection of specimen showed multiple fistulae.

(6) M. 24. R. foot larger than L. Previous infection of great toe, with haemorrhage from foot; pulsations and ulceration. One year before, ligation of anterior and posterior tibial vessels. Later foot a mass of spongy tissue with dilated veins. At operation anterior tibial artery and veins on dorsum of foot ligated; artery was very large; bruit and thrill persisted. At later operation, amputation of leg.

(7) F. 24. Pulsating tumour of the chin, with thrill. External carotid artery ligated and a week later aneurysm dissected and dilated veins ligated. Recurrence 2 years later and mass again removed. 6 months later slight spread to other side, to be treated by radium.

(8) F. 16. L. foot never normal; increased temperature. All toes previously amputated and stump swollen and cyanosed with scab covered sinus; thrill and bruit. Oxygen saturation of venous blood 95%. Posterior tibial and dorsalis pedis arteries ligated. No improvement and foot amputated. A case of multiple aneurysmal varix or cirsoid aneurysm.

PEMBERTON J. and SAINT (35) 1928. Case 3; also reported by MATAS (36a) in 1940. M. 20 in 1919. R. upper limb enlarged; wrist and fingers became ankylosed by rheumatism and suppuration. Bruit in palm of hand and supraclavicular region. At operation, ulnar and radial arteries ligated and noted to be enlarged. One year later, progressive ulceration of hand requiring amputation through mid-forearm. In 1924 returned with pain and swelling above and below clavicle; stump three times normal size tapering towards shoulder. Enormous veins with pulsation and thrill; oxygen saturation of venous blood 90%; increased temperature; enlarged heart.

Matas continued the history. In 1925 he ligated the subclavian artery and vein and internal jugular vein; one week later disarticulation at shoulder. Specimen showed erectile cavernous tissue in which all vessels greatly enlarged; also definite neoplastic hyperplasia of vessels. In 1936 re-appearance in axilla and chest wall. Diagnostic injection of thorotrast, which, incidentally, remained unabsorbed. Tumour in axilla removed en bloc; X-Ray treatment to this area and to area on chest wall. Ultimately good result, with improvement in heart condition.

AKAIWA 1929 quoted by Freund (56). Diffuse phlebectasis of arm.

PATEL (37) 1929. F. 39. Cirsoid aneurysm of scalp. Several operations without cure. Still pulsatile, sinuous tortuous vessels with thrill; increased temperature. Eventually vascular infiltration of cranium developed.

ROCHE (38) 1929. M. 27. Cirsoid aneurysm of scalp above and infront of R. ear. No improvement after preliminary ligation superficial temporal arteries. Then each entering artery ligated and mass removed along with overlying disc of scalp.

WILBUR (39) 1930. M. 43. Arterio-venous fistulae upper limb. Hot spot on hand since birth; increased length of forearm; increased temperature; high oxygen saturation of venous blood. Also multiple arterial aneurysms. After ligation of brachial artery for aneurysm, an embolus lodged in radial artery. Amputation of forearm then carried out.

SCHLOFFER (40) 1930. M. 21. Arterial angioma of neck. Found to be composed of arterialised veins and due to arterio-venous fistulae.

LEWIS /

LEWIS, Dean (41) 1930. Six cases of arterio-venous fistulae:-

(1) M. 21. Large collapsible venous swellings R. upper limb, with bruit and thrill. Hypertrophy of limb. Bradycardia test present. X-Ray examination showed radius perforated by many large vessels. At operation, large thin-walled brachial artery ligated; enormous superficial veins excised and arterio-venous fistulae ligated. Still bruit after operation.

(2) Female. R. forearm enlarged and skin blue; soft compressible swelling, pulsation in veins and thrill. At operation, branch of posterior ulnar recurrent artery found to communicate with veins and ligated; veins dissected away.

(3) M. 1 day old. Vascular soft ulcerated tumour R. arm. Large veins, with bruit. Death after 3 days. At post mortem examination, a cavernous angioma with wide communications between arteries and veins; also patent ductus arteriosus and foramen ovale.

(4) Since childhood, veins dorsum L. hand prominent. Fingers puffy and third and fourth increased in length. Bruit over palm. At operations, communications between radial and ulnar arteries and veins; all communications resected. Dilated veins and bruit persisted.

(5) F. 26. Pulsating tumour of auricle and ear big and purple. Veins in front of and behind auricle and also perforating cartilage. Improvement after excising veins.

(6) F. 44. R. foot and leg enlarged; pain and swelling around heel; thrill and bruit. Electrolysis gave improvement but followed by bleeding. Later several vessels ligated and excised.

KISLICENKO and MILISIC 1931 quoted by Freund (56). M. 19. Phlebectasis of upper limb; atrophy of muscle and bone.

SORREL (42) 1932. F. 13. Hypertrophy, angiomata and enlarged veins lower limb, associated with pain.

THOMSON (43) 1932. F. 33. Hypertrophy L. upper and lower limbs. Angiomata of L. side of body from neck to toes. Severe L. sacro-iliac arthritis, requiring operation for fusion of both sacro-iliac joints.

BLUMGART /

BLUMGART and ERNSTENE (44) 1932. F. 15. Hypertrophy L. upper limb. Phleberteriectasis; enlarged veins, with thrill; cyanosis; small red cutaneous angiomata.

JENKINS and DELANEY (165) 1932. F. 24. Arterial haemangioma of buttock.

KERR (45) 1933. M. 26. Cirsoid aneurysm of scalp. Two stage operation of ligation and excision.

WAKEFIELD (46a) 1926. M. 35. Hypertrophy, angioma and large veins of upper limb.

WAKEFIELD and HINES (46b) 1933. Two cases of congenital hemihypertrophy with widespread naevi.

LASKEY (47) 1933. F. 40. Cirsoid aneurysm of foot. In first metatarsal space, cirsoid vessels of sole communicated with artery.

BRODERICK and ROUND (48) 1933. Two cases of cirsoid aneurysm of maxilla:-

(1) F. 11. Cavernous angioma or cirsoid aneurysm. L. side of face enlarged and bluish, with pulsating spot which started as naevus. X-Ray examination showed extreme absorption of first molars and less of other teeth. Severe bleeding before and after extraction, in spite of pressure, and ligation of external carotid and then common carotid arteries. Death while under anaesthetic.

(2) F. 12 when first seen in 1907. Plexiform angioma or cirsoid aneurysm. Pulsating swelling round R. first upper molar. Severe repeated haemorrhages, especially after extraction. Ligation of common carotid artery. Satisfactory recovery and well in 1933.

SMITH, A.G. (49) 1934. M. 45. Cirsoid aneurysm of scalp.

GOUGEROT and LORTAT-JACOB (50) 1934. F. 12. Hypertrophy, angiomata and varicose veins of lower limb.

DE TAKATS (51) 1932. Five cases of congenital vascular anomaly:-

(1) F. 58. Progressive vascular dilatations of L. arm and hand; attacks of phlebitis; great disability. Previous operation for ligation of radial artery and excision of veins. At further operation, radical excision of ulnar artery and fistulous openings, with almost perfect separation of vessels. Great relief.

(2) /

(2) M. 21. Progressive dilatations of veins of R. wrist and forearm; flushing of R. half of face. At operation, persistent primitive anomalous vessel, showing abnormal histology, was excised, giving relief. No enlargement of deep veins and no arterio-venous fistula found. Diagnosis of phlebectasia.

(3) M. 20. Bluish discolourations entire lower limb, buttock and scrotum of L. side. Rapid enlargement of vascular dilatations. At operation, large mass of spongy dilated vessels extended from skin through deep fascia into muscle; partial removal. Later gluteal portion of angioma injected with skiodan and large vessel visualised, representing connection with general vascular system; treated by sclerosing injections. Histological examination showed large numbers of blood vessels varying from capillaries to large sinuses. Believed to represent retiform stage with arrest of development.

(4) F. 16. Large vascular naevus L. thigh and leg; swollen vessels and repeated bleeding. Limb longer. At three operations, large anomalous vessel removed from thigh to foot on lateral side. No connection with arteries. Specimen consisted of undifferentiated vessels, occluded by thrombus; believed to be localised remnants of primitive capillary net. X-Ray treatment.

(5) F. 42. Localised vascular mass in L. popliteal fossa; excised; specimen showed network of multiple endothelial sinuses. Blood from vessels was bright red and oxygenated. It represents retiform stage with arrest of development.

DE TAKATS and McKENZIE (52) 1934. In addition to above, seven new cases of vascular anomaly.

(6) F. 15. Vascular anomaly face and orbit with progressive vascular dilatation and intermittent exophthalmos. Radium treatment.

(7) F. 24. Vascular anomaly L. lower limb; progressive dilatation; recurrent phlebitis; intermittent claudication. Moderate result with injection treatment.

(8) M. 51. Arterio-venous aneurysm R. leg. Hypertrophy of limb; oedema; ulceration. Excision of aneurysm with good result.

(9) /

(9) F. 50. Multiple angiomata lips and tongue. Swelling, bleeding and gradual spread. Good result with obliterative injections.

(10) F. 32. Phlebectasis of superficial veins of neck and capillary dilatation. Moderate result with excision.

(11) M. 31. Multiple arterio-venous fistulae L. leg. Elephantiasis; dilated vessels; cyanotic toes. Moderate result with excision and injections.

(12) F. 28. Arterio-venous fistulae L. foot. Swelling; increased temperature; ulceration; venous pulsation. Excision with very good result.

COUCH (53) 1935. M. 43. Haemangioma of whole R. upper limb. Limb enormously distended, with tense bluish marks beneath skin; tissues compressible and bones easily palpable through them. Lesion formed a huge cavernous mass communicating with general circulation. X-Ray examination showed frail and irregular bones, and also many phleboliths. Fracture of both bones of forearm developed, but united without difficulty.

ALAJOUANINE, THUREL and HORNET (54) 1935. F. 78. Cirsoid aneurysm upper limb and hand, starting at age 9 on a finger. Hugh dilated and tortuous arteries and veins developed, with pulsation, thrill and bruit. Great increase of temperature; pain; occasional rupture of vessels produced haemorrhage. X-Ray examination showed diffuse osteoporosis and phleboliths. Spontaneous fracture of third finger and ankylosis.

RADULESCO 1935 quoted by Lee, W.E. and Freeman (89). Hypertrophy, varicose veins and cutaneous naevus of lower limb.

DAVID (55) 1936. M. 9. Arterio-venous aneurysm L. hand. Hypertrophy of limb, especially 3rd and 4th fingers; increased temperature; dilated pulsatile veins, with thrill and bruit. Arteriography showed probable fistula in superficial palmar arch. Ulnar artery and digital arteries and veins were ligated and excised. Slight bruit persisted and ligation of radial artery would be necessary later on.

FREUND (56) 1936. F. 8. Genuine diffuse phlebectasia. Fluctuant swelling of shoulder due to enlargement of venous blood spaces; calcified phleboliths. X-Ray treatment.

WEBER (116) 1918. Child 12 weeks old. Haemangiectatic hypertrophy, involving L. upper and lower limbs; diffuse /

diffuse cutaneous angiomata on L. side.

WEBER (117) 1936. M. 17. Widespread superficial telangiectatic naevus of trunk and both lower limbs; varicose veins R. lower limb.

VEAL and McCORD (57) 1936. Seven cases of arterio-venous anastomoses of limbs:-

(1) F. 13. Hypertrophy R. lower limb and labium majus. Gross enlargement R. saphenous vein, blood from which showed oxygen saturation of 86%. Arteriography showed dilatation of smaller superficial arteries which emptied through multiple fistulae into venous channels. No treatment possible.

(2) M. 36. Large varicosities of thigh and leg. Arteriography showed frequent abnormal communications in thigh and leg between arteries and varicosities. Oxygen saturation of venous blood 84%. Treated by sclerosing injections.

(3) M. 32. Large varicosities L. cubital fossa with thrill and bruit. Oxygen saturation of venous blood 81%. Arteriography showed single large communication between upper end of radial artery and superficial varices. Treatment refused.

(4) F. 71. Large varicosities entire L. lower limb; bright red blood in veins. Arteriography showed abnormal arterio-venous communications. Treated by ligation of veins and injections.

(5) M. 24. Large dilated veins upper limb. X-Ray examination showed atrophy of 4th and 5th metacarpals and 5th finger. Arteriography showed direct arterio-venous communications in many places. Ligation of vessels unsuccessful, and followed by amputation through arm.

(6) M. 37. Large tortuous varicosities R. leg. Oxygen saturation of venous blood 90%. Arteriography showed multiple communications between arteries and veins. Injection treatment.

(7) M. 23. L. arm slightly smaller. Oxygen saturation of venous blood 85%. Arteriogram showed dilated vascular pockets emptying directly into veins.

PEABODY (58) 1936. F. 13. Hypertrophy L. upper and lower limbs; angiomata both sides.

KIDNER (59) 1936. Four cases of cavernous angioma of lower /

lower limb:-

(1) F. 24. Large varicosities L. leg and tender compressible swelling. At operation huge mass of dilated veins removed from under deep fascia. Muscle infiltrated.

(2) F. 10. Numerous enlarged veins L. leg and foot; increased circumference; increased temperature. Also severe congenital flat foot. At operation, tumour lay under gastrocnemius and was composed of dilated blood spaces. Following operation, a thrill and a bruit developed in engorged foot due to arterio-venous connection. X-Ray treatment.

(3) M. 39. Enlargement R. calf with enlarged veins. At operation, mass of distended, irregular, thin-walled vessels removed from under deep fascia.

(4) M. 8. Swelling and enlargement of leg. At operation, deep fascia penetrated by dilated vessels and mass of vessels, infiltrating muscle, removed.

GILMOUR and BOLAM (60) 1937-1938. Two cases of arterio-venous fistulae of foot:-

(1) M. 13. Indolent ulcer dorsum and second toe L. foot; prominent pulsatile veins; purple naevus foot and toes; increased size of limb; increased temperature; thrill and bruit over femoral and posterior tibial arteries. Arteriogram showed dense network of small vessels in foot and multiple arterio-venous communications. X-Ray examination also showed periostitis second toe. Amputation.

(2) F. 40. Chronic ulcer second toe R. foot; purple discolouration; large pulsatile veins; bruit over saphenous vein and posterior tibial artery. Arteriogram similar to above case. Attempt at local removal of aneurysmal communications unsuccessful. One month later gangrene, necessitating amputation.

HOLMAN (61) 1937. M. 30. Haemangioma R. hand, exhibiting characteristics of acquired arterio-venous fistula:- arterial blood in dilated veins; increased calibre of radial artery; increased general blood pressure on closure of arteries in forearm proximal to angioma; marked increased length of bones of forearm. Also thinned-out red skin over tumour; angioma practically limited to superficial tissues /

tissues. Excised specimen consisted of numerous dilated endothelial-lined blood spaces in a mass of fibrous tissue.

CHANDLER (62) 1937. Three cases of hemi-hypertrophy:-

(1) F. small child. Hypertrophy upper limb and haemangioma.

(2) M. child. Hypertrophy lower limb and haemangioma.

(3) F. infant. Hypertrophy lower limbs, haemangioma, and lymphangioma.

BELUFFI (63) 1937. M. 29. Cirsoid aneurysm of buttock, due to multiple arterio-venous anastomoses.

ROSENAK (64) 1937. M. 33. Arterio-venous fistulae L. Upper limb. Forearm enlarged; tortuous veins with bruit; bradycardia test positive; arteriography showed dilated arteries. At operation, ligations of radial and interosseous arteries.

PAUTRIER and LANG (65) 1937. M. 23. Hypertrophy R. lower limb and R. side of scrotum; large varicosities; haemangioma and lymphangioma.

RUNDLE (66) 1937-1938. M. 45. Cirsoid aneurysm of scalp. Arteriography with thorotrast showed mass of convoluted dilated vessels, with rapid emptying into sigmois sinus. After preliminary ligation of superficial temporal arteries, mass of thin-walled vessels dissected off scalp flap.

TOURAINE, DUPERRAT and BAUDOUIN (67) 1938. M. 9. Increased girth lower limb; varicosities and angiomata.

PEYTON and LEVEN (68) 1938. Arterio-venous aneurysm of nose.

WISE and LISANSKY (69) 1938. M. 33. Arterio-venous fistula. Mass of enlarged veins from L. nipple to L. foot; oxygen saturation of venous blood increased; limb hypertrophied; increased temperature; slight bone atrophy.

WRIGHT, A.D. (70) 1938. M. 36. Arterio-venous aneurysm R. thigh. Extensive angioma of R. lower limb; large veins, which developed pulsation; ulceration. Arteriogram showed large feeding vessels passing to pulsating mass in thigh. Several operations, at which many arterial branches ligated and veins excised. Thereafter, still ulceration and slight pulsation.

WARD /

WARD, G.E. and JONAS (71) 1938. M. 82. Pulsating angioma of hand; developed metastases in glands. Also had carcinoma of gall bladder.

HALSTED (15) 1919; also reported by REID (72) 1925 - (case 29).

Female aged 11 in 1911. Three days after birth, buzzing and throbbing discovered in R. side of neck. At age 8 swelling noted; also pain and occasional dizzy spells. Below lobule of ear, a pulsating swelling $3\frac{1}{2}$ c.ms x $4\frac{1}{2}$ c.ms with thrill and continuous bruit, which disappeared on occlusion of carotid artery. At operation in 1911 by Halsted, fistulous track between external carotid artery and a large vein was excised; this artery and common carotid were dilated, but internal carotid artery small. Still slight pulsation, thrill and bruit.

In 1918 condition worse than ever. At second operation by Reid, an aberrant artery, forming a fistulous connection, was excised; again moderate improvement. In 1922, much more extensive; lesion now received blood from L. carotids as well as from R.

REID (72) 1925. Three cases of vascular anomaly, excluding intracranial and above cases:-

(1) (Case 28). F. 23. Cirsoid aneurysm lower eyelid; excised. Communicating artery was from ophthalmic artery. Good result.

(2) (Case 30). M. 18. Arterio-venous aneurysm of neck. Large lobulated pulsating mass filled R. supraclavicular fossa, hung over clavicle and extended below scapula. Huge veins neck and scalp, with pulsation, thrill and bruit. R. arm bigger. At first operation, vessels ligated and part of mass removed from neck. Over a year later, at second operation, clavicle removed; internal jugular and subclavian veins ligated; connection between subclavian vein and aneurysm ligated and divided; large fistula found between subclavian artery and mass of veins; subclavian artery and thyroid axis ligated. Still excellent result four years later.

(3) (Case 31). F. 35. R. leg hypertrophied; pigmented spots; congenital varicose veins, which began to pulsate, with thrill and bruit; increased temperature. X-Ray examination showed vacuolated areas in tibia. At operation, popliteal artery now appeared too long and kinked. Five /

Five days later gangrene developed, necessitating amputation; popliteal artery found to have ruptured. Specimen showed branches of anterior tibial artery opened into large openings in cortex of tibia; many with little saccular aneurysms; large veins emerged from openings in cortex, and within tibia were large vascular cavities, lined with endothelium which connected with arteries and veins.

REID (76) 1931. F. 13. Venous angioma L. lower limb. Bluish discolouration from buttock to foot; otherwise limb paler. Limb smaller; increased temperature. On standing after lying down, vessels became dilated and child complained of dizziness; pulse rate increased and systolic blood pressure decreased. Probable that great deal of blood was shunted into angiomatous area, so that dizziness was due to anaemia of brain.

REID and McGUIRE (77) 1938. Six cases of arterio-venous aneurysm:-

(1) (Case 9). F. 1. Extensive cirsoid aneurysm lower limb. Marked hypertrophy; thrill and bruit; blue discolouration; ulceration of calf. At operation femoral artery and vein ligated; mid-thigh amputation later. Specimen showed venous dilatations, thrombosis, many vessels and involvement of muscle.

(2) (Case 16). F. 24. Large arterio-venous haemangioma R. forearm and hand. Irregular swelling, increasing on dependency; blue discolouration; large veins; phleboliths. At operation, lesion involved all volar muscles and nerves, and space in front of interosseous membrane; venous blood definitely arterial in colour.

(3) (Case 17). M. 34. Cirsoid aneurysm L. arm. Hypertrophy; swelling; pain; disability; increased temperature; increased venous pressure; Wassermann reaction positive. Arteriogram showed very large arteries. Improvement after ligations and excisions of superficial veins; to be repeated and to have sclerosing injections.

(4) (Case 22). F. 14. Cirsoid aneurysm upper limb. Hypertrophy; swellings; large superficial veins, with bruit; disability. At operation, partial excision of aneurysm from muscles, tendons and nerves; following by sclerosing injections.

(5) (Case 25). M. 19. Cirsoid aneurysm below L. ear. At /

At operation, multiple communications found between external jugular vein and branches of external carotid artery, chiefly occipital; ligations of external carotid and occipital arteries; division and twisting of external jugular vein. Good result.

(6) (Case 30). M. 19. Spontaneous multiple cirsoid aneurysms - one in neck, two in L. forearm, one on dorsum L. foot. Cardiac enlargement. At operations, excision of cirsoids of forearm and foot; partial excision of cirsoid in neck, followed by ligation of R. external carotid artery; slight bruit persisted. Arterio-venous communications definitely demonstrated at operation.

SEEGER (78) 1938. M. 9. Arterio-venous fistulae R. leg. Large veins; dusky on standing; increased temperature; swelling of ankle. Arteriography showed rapid escape of opaque medium into veins. Increased oxygen saturation of blood from vein in popliteal fossa. At operation, branch of profunda femoris artery entered large venous mass; several ligations of arteries and veins.

O'NEIL (79) 1939. Thirteen cases of arterio-venous fistulae of limbs:-

(1)-(12). Six cases showed lengthening; one case showed shortening of an arm; all showed increased temperature; two had doubtful cardiac lesion; most showed increased oxygen content of venous blood; two showed bruit and thrill; several showed ulceration or eczema.

(13) F. 23. Varicose veins R. leg and thigh; haemangioma thigh; increased circumference of limb; increased oxygen content of venous blood. At operation, eight separate fistulae found between femoral artery and vein; fistulae ligated and divided, remaining veins sclerosed with injections. Gradual subsidence of swelling and disappearance of angioma.

NEWSON (80) 1939. M. 18. A case of Sturge's disease. Port-wine capillary naevus L. side face and neck, crossing mid line; intracranial calcification; R. hemiplegia; cupping of L. optic disc, with poor vision. Also showed hypertrophy, naevus and varicosities L. upper limb, suggesting arterio-venous fistulae.

PACK (81) 1939. Diffuse haemangiomatosis L. hand and foot; hypertrophy of bones of L. foot. X-Ray examination of foot indicated haemangioma involving bone.

ABRAMSON (82) 1939. F. 18. Arterio-venous aneurysm R. lower limb. Hypertrophy; swelling on standing; thrill and bruit; ulceration; pigmentation; increased temperature; cardiac hypertrophy. Fistulae probably in pelvic vessels.

NEMENOV (83) 1939. M. 37. Angioma of radius and ulna; several previous fractures of forearm; vascular anomaly of soft parts of upper limb.

WERTHEIMER (84) 1939. F. 18. Hypertrophy, angiomata and large veins upper limb; increased temperature.

TAVERNIER (85) 1939. Child. Hypertrophy, angiomata and large veins lower limb.

HOMANS (86) 1939. Three cases of vascular anomaly:-

(1) Child. Angiomata and dilated veins lateral side leg and foot. Lengthening of limb at first, followed later in growth by equalisation.

(2) M. 21. Probably a venous angioma. Dark patch of skin L. thigh; large incompetent varicose vein from ankle to gluteal fold; faint bubbling sound on auscultation above knee. At first operation, greater part of vein excised; vein gave off many small branches connecting with naevus; tissues very vascular and healing delayed by haematoma. Occasional attacks of severe bleeding during next ten months. At second operation, tortuous plexus of veins excised, superficial and deep to deep fascia. Later sclerosing injections.

(3) M. 19. Arterio-venous fistulae L. upper limb. Dilated veins elbow and forearm, which began to pulsate; thrill and bruit; increased circumference of forearm; increased temperature; increased oxygen content of venous blood in forearm. Closure of fistulae by proximal pressure on arteries of limb produced reduction in pulse rate of 13 per minute and a generalised increase of systolic and diastolic blood pressure. At operation, brachial artery twice normal size, narrowing to normal 2 c.ms above bifurcation; multiple fistulae found then and at later operation, and also shown on arteriogram; fistulae came off brachial, ulnar recurrent, dorsal and volar interosseous arteries. Later dilated brachial artery ruptured twice, being first ligated /

ligated and then ligated and divided, along with its vein. Considerable improvement thereafter.

WATSON and McCARTHY (164) 1940. Blood vessel tumours - five selected by me:-

(1) F. 16. Racemose type of haemangioma. Cirsoid pulsating mass upper lip. Histological examination showed thin-walled vessels, communicating directly with a thickened arteriole, with cellular proliferation in its walls.

(2) M. 60. Racemose type of haemangioma. Onset at age 20. Soft, bluish, cavernous, pulsating, compressible mass, involving L. side of face and bulging into oral cavity.

(3) F. 14. Diffuse systemic haemangioma entire L. lower limb; hypertrophy of limb; dilated superficial vessels; spongy consistence. Also had nephrectomy for perithelial angioma R. kidney.

(4) Infant five months old. Soft, bluish, pulsating mass in subcutaneous tissues of face; complete regression after two injections of sclerosing solution.

(5) M. five months old. Diffuse, systemic haemolymphangioma lower limb.

LEE, W. E. and FREEMAN (89) 1940. Three cases of extensive venous angiomata of lower limb and varicose veins:-

(1) F. 17. Complaint of a sore, swollen R. foot and attacks of syncope on standing. At age 12, slight thickening of limb noted. Large angioma from iliac crest to foot. Recent attack of phlebitis R. leg; after recovery from this, first noticed angioma became turgid and suffused in erect posture. Varicose veins which filled from a communicating vein and from long saphenous vein; angioma filled rapidly through these veins, but reflux could be prevented by a venous tourniquet. On standing, blood pressure fell from 135/85 to 90/70, and pulse rate increased from 60 to 152 per minute. Upon release of tourniquet, which had completely occluded circulation above knee, volume of leg in one minute increased by 200 c.c. measured by displacement of water; on normal side increase was only 25 c.cs. Specimens of blood from veins of both legs and both femoral veins showed same colour. At operation, R. long saphenous vein ligated at junction with femoral vein, along with four large /

large branches; ligation repeated at lower level. Result was freedom from symptoms and decrease in size of angioma.

(2) M. 23. Complaint of pain and repeated attacks of phlebitis in varicosities R. leg. Extensive angiomata R. lower limb, R. half of scrotum and penis. General osteohypertrophy both feet, but particularly R. 2nd, 3rd and 4th toes and L. 2nd and 3rd toes. Varicose veins R. leg since age 12, subject to thrombophlebitis with such pain that severe flexion contracture of knee developed. Four previous operations for veins and deformity. Varicose veins were in free communication with large blood sinuses on postero-lateral aspect thigh and leg; long saphenous vein not involved and point of incompetence was in region of gluteal veins; veins visualised by injection of 30% diodrast. At operation, two large veins divided at lower border of gluteus maximus; tissues very vascular and bleeding controlled with difficulty. Condition of veins improved and less increase in pulse rate on standing.

(3) M. 19. At birth multiple vascular and other congenital anomalies. Hypertrophy of bones of both feet and L. upper limb; fusion of two fingers L. hand; hypertrophy L. breast and increased growth of hair over it. Large angiomata both lower limbs; penis and scrotum and lower left part of abdomen; varicose veins both lower limbs; angiomata became suffused with blood on standing. Blood pressure fell from 120/70 to 80/60 on standing and pulse rate increased from 65 to 144. Volume of L. leg increased by 475 c.cs. within one minute of release of tourniquet above knee. No abnormality of oxygen saturation of venous blood. At operation L. long and R. short saphenous veins ligated; further operations planned. Marked improvement.

COLLEY, R.D. (88) 1940-1. Six cases of cirsoid aneurysm:-

(1) F. 15. Lesion of scalp and face. Red mark at birth, slowly increasing in size, which began to pulsate at age 14 and grow rapidly. Recent ulceration and haemorrhage. Treated by ligation of main arteries, followed by injection of coagulants for 3 years. Improvement followed and pulsation arrested; still cavernous mass and scar tissue on forehead.

(2) M. 29. Lesion of scalp and cheek. Began at age 2 /

2 with "pimples" below L. eye; then began to swell. At age 5 ligation of L. common carotid artery, causing right-sided hemiplegia and mental impairment. At age 29 began to pulsate and increase rapidly. Treated by ligation of entering arteries as a preliminary to injection, but followed by deep coma and death.

(3) M. 35. Swelling R. cheek and upper lip since childhood; recently began to pulsate and increase. Treated by ligation of entering arteries and excision of mass of cavernous tissue. Complete relief.

(4) M. 32. Widespread lesion R. thigh, with distended, pulsating veins; capillary angioma and increased size. Treated by ligation of arteries of supply and excision of cavernous tissue and distended veins; great improvement.

(5) F. 46. Since birth, pulsating swelling L. thumb, extending into veins of forearm. Treated by ligation of artery and excision of veins; complete relief.

(6) M. 39. Diffuse, pulsatile swelling L. hand, starting on index finger in childhood. Treated by ligation of palmar arteries and excision of veins; relief.

WRIGHT, L.T. and LOGAN (90) 1940. M. 28. Arterio-venous aneurysm R. upper limb. When dependent, limb about twice as large as opposite limb, but on elevation shrank to about normal. Veins very large and tortuous; thrill and bruit; increased temperature. Blood Kahn reaction strongly positive. X-Ray examination showed bones of arm and hand larger but rarified, and with large nutrient foramina; also atrophy of bones of wrist, and vacuoles in bones of hand due to pressure of varices. Arteriogram and venogram showed dilated tortuous vessels but no definite arterio-venous communication. Diagnosis made of arterio-venous aneurysm of radial artery. At operation, radial artery exposed and thin-walled pulsating vessels ligated and excised. Eleven months later, oxygen estimation of venous blood showed it almost arterial in character. At second operation, brachial artery and median cubital vein ligated and excised; and also soft spongy subcutaneous masses. Histological examination showed no evidence of neoplasm. Two months later, amputation through humerus.

ECKHOFF /

ECKHOFF (91) 1940-1. M. 26. Cirsoid aneurysm chest wall; large pulsating swelling since birth. Treated by many operations:- ligation of entering arteries; transfixion; excision and skin grafting; also radium. Marked improvement.

HORTON (92) 1932. Twenty-two cases of hemihypertrophy of extremities associated with congenital arterio-venous fistula. An additional case, case 22, omitted here, as given in more detail by Horton and Ghormley (95) 1935.

(1)-(21), (23). All cases showed hypertrophy, and all but five an increase in length; all showed dilated enlarged vessels; all but one showed increased temperature. Oxygen estimations of venous blood made in all but four cases, and with conclusive results; in three cases, however, it was necessary to examine blood from femoral veins. Other features present in some cases were a thrill, a bruit, a positive bradycardia reaction, cardiac hypertrophy, arthritis, bone atrophy or destruction.

HENCH and HORTON (93) 1933. Two cases of arterio-venous fistulae of intercostal vessels. F. 30 and F. 33. In both loud bruit audible over 7th and 8th ribs.

HORTON and GHORMLEY (94) 1934. Two cases of arterio-venous fistulae:-

(1) M. 14. Arterio-venous fistulae L. lower limb. Circumference slightly decreased; increased temperature. Two previous operations, tissue removed at which times showing microscopic structure of cavernous haemangioma. Arteriography, using 10 c.c of thorotrast, showed rapid filling of femoral vein and an arterial blood supply to angiomatous masses in lower third of thigh and in calf.

(2) F. 7. Further details also given by same authors in 1935. Arterio-venous fistulae L. lower limb. Hypertrophy; increased temperature; blood removed from femoral vein showed high admixture of arterial blood. Arteriography showed femoral artery ended in network of vessels in lower part of thigh; also rapid filling of a large vein in popliteal space. In 1935 femoral artery exposed and fistula easily identified and ligated. Three weeks later sudden discomfort in leg with rapid increase in temperature. Venous blood in region of heel showed high oxygen saturation. Apparently new fistula had opened near ankle.

HORTON /

HORTON and GHORMLEY (95) 1935. Three cases of arterio-venous fistulae:-

(1) M. 60. Spongy swelling R. index finger with commencing gangrene; enlarged veins; increased temperature of hand. X-Ray examination showed erosion of middle phalanx. Oxygen saturation of venous blood:- R. index 95%; L. hand 73%. Arteriogram, using thorotrast, showed abnormal arterio-venous communications in R. index. Finger amputated; dissection showed 3 arterio-venous fistulae. Thirteen days later oxygen saturation of venous blood was same in both hands.

(2) M. 40. First diagnosed as traumatic arterio-venous fistula and reported as such by Yater in 1928. History of injury to R. hand at age 20, but at that time already increased growth of bones of forearm; probably trauma merely aggravated a congenital condition. R. middle finger already amputated before 1935. Present condition showed prominent veins of dorsum of hand and forearm and a fluctuant, pulsating bluish mass at base of 4th finger, with bruit. At operation, mass was explored and digital branches of superficial palmar arch were ligated; wound took eight weeks to heal and lesion became bigger. Then increased temperature and positive bradycardia reaction. Oxygen saturation of venous blood:- R. arm 95%; L. arm 59%. Arteriograms, using thorotrast injected into brachial artery, showed that opaque material had not entered fingers and had been short-circuited into veins through abnormal arterio-venous communications in hand. At operation, R. 4th finger and V-shaped portions of 3rd and 4th metacarpals were excised; primary healing took place with return of circulation to normal. Serial microscopic sections of specimen revealed many direct communications between arterioles and venules. Three weeks later, oxygen saturation of venous blood was reduced on R. arm, but still higher than on L. arm; this indicated still small arterio-venous fistulae existed. Hand now useful for work. The heart, which previously had been dilated, was now decreased in size.

(3) M. 41. Additional case with no details. Arterio-venous fistulae L. leg, successfully treated by injections of sclerosing solution.

SMITH /

SMITH, F.L. and HORTON (96) 1937. F. 29. Arterio-venous fistulae L. upper limb. Enlarged vein L. forearm, noted at birth. Slight increase in oxygen saturation of venous blood. Arteriogram showed many arterio-venous fistulae between inter-osseous artery and vein. Great improvement after injections of sodium morrhuate.

HORTON and HEMPSTED (97) 1938. Arterio-venous fistulae middle ear and external auditory meatus. (Reference not examined).

WARD, C.E. and HORTON (98) 1940. Thirty-three cases of arterio-venous fistulae; in addition authors described five cases in the limbs which had been previously reported, and four intracranial cases.

(5)-(8). Four cases involving scalp, face and neck. Case (5) showed a lesion on the R. side of neck, face and scalp and R. ear:- external cavernous haemangioma and birthmarks; bruit; thrills; increased temperature; treated by ligation of external carotid and transverse cervical arteries and excision of dilated vessels.

(9)-(17). Nine cases involving upper limb. Dilated tortuous vessels present but bruit or thrill absent in all cases; in almost all limb larger. Case (12), a boy of 9, showed an enlarged L. hand with birthmark and increased oxygen saturation of venous blood; treated by multiple excisions and ligations and radium. Result was improvement, but limb was left $2\frac{1}{2}$ c.ms shorter.

(20), (21). (23)-(26), (29)-(42). 20 cases involving lower limb. In almost all cases increased size; increased temperature; angiomata, dilated veins; in some, raised oxygen saturations and arteriograms. Case (34) showed eventual shortening of a previously enlarged limb as result of irradiation treatment. Case (35) was very uncommon in that malignant change took place, producing death from widespread metastases.

In addition to the above, two cases of hemihypertrophy were reported, with involvement of face, upper limb and lower limb of one side, and with widespread capillary angiomata.

STAUFFER, ARBUCKLE and AEGERTER (100) 1941. M. 19. Polyostotic fibrous dysplasia with cutaneous pigmentation and congenital arterio-venous aneurysm. Bony /

Bony enlargement L. frontal region and L. jaw. L. upper limb increased in diameter, but almost useless due to deformities from old fractures, ankyloses and distorted hand. L. lower limb shorter, and deformed by coxa vara, genu valgum and genu recurvatum. Increased temperature L. arm and thigh; pigmentation of thorax. R. arm slightly swollen. L. eye proptosed, with oedema of disc. Heart greatly enlarged. Compression of L. axillary or L. femoral artery caused fall in pulse rate of 20 per minute. Thrills and bruits L. upper limb and thigh; dilated tortuous, pulsatile veins L. arm. X-Ray examination of L. humerus showed great expansion, thin irregular cortex, bowing and appearance like small cysts; similar changes in other bones. Oxygen saturation of venous blood:- L. forearm 90%; R. forearm 34%. Biopsy showed medullary cavity occupied by solid, gritty, fibrous tissue.

HIRSCHFELD (101) 1941. M. 24. Plexiform haemangioma L. hand. Soft elastic swelling and large tortuous veins. X-Ray examination showed rarefaction of phalanges, with honeycombed appearance. Treated by injections of sodium morrhuate.

WATKINS (102) 1941. F. 8. Arterio-venous aneurysm R. lower limb. Hypertrophy and increased temperature. Several pulsating vessels over knee and leg, and distension of superficial veins. Two days before examination, milky discharge from pin point opening in thigh; this fluid contained many lymphocytes and was believed to be the result of lymphangiectasis; discharge stopped spontaneously and did not re-appear. Positive bradycardia re-action.

LAIRD (103) 1941. F. 6. Deep cavernous haemangioma of neck. Aspiration yielded unmixed blood. At operation, a tortuous cirsoid mass of vessels was exposed and excised. It received an abundant blood supply from the region of the carotid sheath and was composed of dilated veins containing phleboliths. Histological examination showed appearances of cavernous haemangioma.

KLEINBERG (104) 1942. F. 19. Angioma R. foot. Soft, elastic, non-pulsatile swelling on plantar surface. X-Ray examination showed a destructive lesion of cuboid and 3rd cuneiform, producing cystic areas. At operation, a mass of varicose veins, i.e. an angioma, was found between the layers of muscle. These communicated with bone and with vessels which entered from all directions; many vessels ligated and mass removed. Phleboliths present. X-Ray treatment given thereafter.

STEINBERG /

STEINBERG, GRISHMAN and SUSSMAN (105); also TOUROFF (106) 1942. F. 13. Arterio-venous aneurysm L. upper limb. Pulsatile swelling L. side of neck and supraclavicular region, with thrill and bruit. L. upper limb showed hypertrophy; pulsating, superficial veins and increased temperature. Bradycardia re-action marked, pulse rate falling from 95 to 52 per minute. X-Ray examination revealed replacement of entire shaft of humerus by irregular vacuolisation, due to vascular channels. Angiocardiography, using diodrast, demonstrated probable site of arterio-venous fistula to be at or above origin of axillary vessels. Several operations without success. Condition of heart becoming worse and finally ligation of first part of L. subclavian artery carried out, using a trans-thoracic, trans-pleural approach. Gangrene of wrist and hand developed, requiring amputation. Condition of heart improved after operation.

LUKE (107) 1940. Three cases of arterio-venous fistulae:-

(1) F. 15. L. lower limb increased in circumference but not in length; numerous veins; increased temperature. Arteriography demonstrated two fistulae between femoral vessels. No treatment.

(2) F. 68. Condition noted at age 2. Vascular tumour and enlarged tortuous veins R. 4th finger, hand and forearm. Pulsation in veins; bruit; increased temperature; radial and ulnar arteries much enlarged. Arteriography also showed extensive degree of arterio-venous communication in 4th finger. No treatment.

(3) M. 50. Enlarged R. foot; enlarged veins in leg; loud bruit on dorsum of foot; pigmentation and ulceration of leg. Arteries much enlarged, and arteriography in addition showed a large mass of arterio-venous communications in sole. At operation, dorsalis pedis and posterior tibial arteries ligated; a threat of gangrene present thereafter, but ultimately good result.

LUKE (108) 1942. F. 26. Arterio-venous fistula of L. pinna, forming a pulsating tumour. Treated by multiple ligations and excision.

PRATT (109) 1942. Two cases of arterio-venous fistulae:-

(1) Large mass of blood vessels in suprahyoid region, fed by L. lingual, facial and inferior thyroid /

thyroid arteries, and many abnormal connections from R. external carotid artery. At operation, treated by extirpation of the three arteries on L. side and R. external carotid artery, thereby closing fistula.

(2) Entire upper limb, shoulder and chest wall involved in large arterio-venous fistula. Showed malignant change, similar to that described by Matas.

FULTON and SOSMAN (110) 1942. Four cases of venous angioma of skeletal muscle:-

(1) F. 23. Large venous plexus in elbow region; attacks of thrombophlebitis; phleboliths. X-Ray examination, after injection of diodrast into veins, showed a plexus, with large venous lacunae. X-Ray treatment inconclusive.

(2) F. 32. Soft, tender mass in elbow region, covered by faintly blue skin; phleboliths. At operation, tumour dissected off deep fascia; made up of blood vessels invading triceps and growing round ulnar nerve. Histological examination showed appearances of cavernous haemangioma.

(3) M. 18. Large veins L. hand and forearm; attacks of swelling and pain; limb swollen, blue, tender and warm; phleboliths; minor subcutaneous haemorrhages. X-Ray examination of hand showed peculiar honeycombed appearance of bones believed to be due to angioma. X-Ray treatment inconclusive.

(4) M. 20. Tender swelling sole of R. foot; phleboliths. At operation, obvious angioma found, composed of large tortuous vessels, too extensive for dissection. Slight improvement after X-Ray treatment.

BOWER, DITKOWSKY, KLIEN and BRONSTEIN (111) 1942. M. 9. Arterio-venous angioma of L. mandible and L. retina. L. side of face fuller and warmer and with prominent veins and faint blue discoloration; thrill and bruit over this area. X-Ray examination showed several cystic areas in mandible which disappeared spontaneously in next nine months. L. eye blind due to arterio-venous abnormality of retinal vessels.

SHUMACKER (112) 1942. M. 33. Congenital anomaly of R. lower limb, associated with diffuse haemangioma of subcutaneous tissues and skin, subcutaneous fibrosis, deficient lymphatic drainage, elephantiasis and hypertrophy of limb. Small blebs on skin of /

of leg which would rupture and discharge large quantities of clear fluid. Increased temperature. Increased sweating which necessitated lumbar ganglionectomy. Limb 8 c.ms longer and much increased in girth. Definite bruit over femoral artery. Treated with success by Kondoleon type of operation, removing large amount of subcutaneous tissue.

CARLETON, ELKINGTON, GREENFIELD and ROBB-SMITH (201) 1942. Description of Maffucci's Syndrome (dyschondroplasia with haemangiomata). Two personal and twenty-two other cases discussed, with mention of arterio-venous anastomoses in one case.

EALING (218) 1943. Male infant. Haemangioma of arm causing delay in delivery and neo-natal death. Great enlargement of limb, extensive varicosities, thrill and bruit; enlarged heart.

FINLEY and SHAFFER (219) 1943. Congenital arterio-venous aneurysm arising from superficial circumflex iliac vessels. (Reference not examined).

KULCHAR (220) 1944. Child. Cavernous angioma producing gigantic enlargement of whole R. lower limb.

ELMSLIE (221) 1928. Arterio-venous aneurysm brachial artery; cavity in humerus, containing accessory aneurysmal sac.

LOVE and HORTON (222) 1944. M. 20. Three nodules in elbow region since birth; ulnar nerve paralysis produced. Arteriogram showed arterio-venous fistulae in relation to branch of brachial artery; arterial blood in veins. Successful excision of nodules and fistulae.

S E C T I O N F O U R.

A DISCUSSION ON THE CLINICAL FEATURES.

THE CLINICAL DIAGNOSIS.

As mentioned in the Introduction, the nomenclature of the congenital vascular anomalies under discussion is confused and inaccurate, and different titles have been applied to the same type of condition. A most important and controversial point is whether a given lesion is a developmental malformation of the blood vascular system or a haemangioma, by which is indicated a true tumour. The pathology thus being uncertain, it follows that accurate clinical diagnosis is difficult. From the clinical point of view, it would appear that most of the recorded cases have been classified as various types of haemangioma, pure venous abnormalities, cirsoid aneurysms, and arterio-venous aneurysms of the classical type. There is, however, no hard and fast line of distinction between these types, one fading imperceptibly into the other, and modern authors, such as Reid (73) and De Takats (51), have tended to emphasise the essential similarity. In addition, the uncommon condition of glomangioma is known rarely to give rise to appearances which may be indistinguishable from the above, and there have also to be considered certain other telangiectatic conditions.

Though all the conditions under discussion are considered to be congenital, there are variations in the time at which their presence is first appreciated and in the speed of their further development. In eleven of my cases and in the majority of reported cases, an abnormality was noted at birth, usually the increase in the size of a limb or a form of haemangioma. The difference in the size of the limbs tends to become more pronounced after a few years. The angiomatous lesion may be quite small at first but shows a great tendency to increase in intensity in later childhood, at puberty or even in adult life. Varicose veins may be noted at birth but more often become apparent a few years later. A fairly common finding is that trauma instituted the onset of severe progressive changes from a previously quiescent state, and it is sometimes difficult to determine whether one is dealing then with a congenital anomaly or with an acquired or traumatic cirsoid or arterio-venous aneurysm. The case reported first by Yater and subsequently by Horton /

Horton and Ghormley (95) was an instance of this problem. A similar lack of decision may be unavoidable, especially with a cirsoid aneurysm of the scalp, when an injury during the actual process of birth may give rise to a lesion indistinguishable from a true congenital lesion.

Examination of reported cases of congenital vascular anomalies shows that one particular group of signs is common to all varieties. Three most striking signs are hypertrophy of a part, usually a limb, widespread capillary haemangiomata and extensive varicose veins, and, though described by some authors as typical of one class of lesion only, they have in fact been reported in all varieties. Their occurrence in apparently diverse states seems to be good evidence that the underlying pathology is essentially similar, and their association, as pointed out by Klippel and Trenaunay (11) in 1900, is certainly no coincidence. Other features occurring jointly are those related to local and general circulatory changes. Brief mention will now be made of the typical clinical features of each of the recognised varieties of vascular lesion.

Diffuse phlebectasis is essentially a venous abnormality and is known by several names such as diffuse phlebectasia, extensive venous angioma, the syndrome of Klippel and Trenaunay, the syndrome of Parkes-Weber, or the syndrome of osteohypertrophy, varicose veins and angiomata. Though most typically found in the lower limb, it can occur elsewhere. In its common site, the essential features are hypertrophy of the bones and soft tissues, extensive capillary or cavernous haemangiomata, and severe varicose veins, but variations have been described in which one of these might be absent. There is an increased local temperature and there is a tendency to chronic ulceration of the leg or toes. Interesting cardio-vascular effects, believed to be due to the loss of blood into the veins and the angiomata on standing, are an increase in pulse rate, a rise in the diastolic and a fall in the systolic blood pressure. In true phlebectasis, it is assumed that the angiomata fill by abnormal connections with the veins and therefore a normal oxygen content of the venous blood and a normal arteriogram are present. Lee, W.E. and Freeman (89) have given an excellent account of phlebectasis. Recently, however, doubt has been cast on this diagnosis in many cases, and cases exactly similar clinically have shown a high oxygen content of the venous blood, indicating the presence of arterio-venous /

venous communications. Horton (92) and his associates (98)(99) have been foremost in emphasising this latter fact.

The term venous angioma is also applied to what seems no more than a localised collection of veins, similar in appearance to the common types of venous varicosities, and differing only in a congenital or early onset and perhaps in an unusual situation. Such a lesion may be solitary or it may be associated with widespread and extensive vascular abnormalities, as, for example, in Case 7, where the lesion in the healthy upper limb might well be called a venous angioma. It has been suggested that the term venous angioma be applied to small localised lesions and the term phlebectasis to the more diffuse lesions.

Cirsoid aneurysm is a term applied to varying appearances and is also known by many other names such as pulsating, plexiform or arterial angioma, aneurysm by anastomosis and racemose aneurysm. Arterial blood circulates in the aneurysm which is considered due to multiple arterio-venous communications. The lesion is found most typically in the scalp, involving especially the superficial temporal artery. The term is applied, however, to lesions in any situation involving smaller arteries, as in the hand or foot, but unfortunately is also used as an alternative designation for extensive arterio-venous aneurysms. The cirsoid aneurysm forms a localised, pulsating mass of vessels which on palpation has been likened to a bag of writhing worms. An angioma is present in the overlying skin, the surface temperature is increased, a bruit and a thrill are present and the Nicoladoni bradycardia test is positive. Hypertrophy of the affected part may occur. In the later stages, the lesion becomes very extensive and may occupy most of the scalp or a large portion of a limb, the neck or the trunk.

The arterio-venous aneurysm of the classical type is known also by the same alternative names as the cirsoid aneurysm. The term may be restricted to lesions at or near the root of a limb involving the subclavian, axillary, iliac or femoral vessels. It is also applied to lesions of any main arterial and venous trunks, and sometimes to those of smaller arteries, thereby covering the scope of the cirsoid aneurysm. However, no matter the site at which the first obvious fistulae were present, extension tends to take place, due to the opening up of new fistulae. In a limb, the most prominent features are hypertrophy of the bones and soft tissues, extensive haemangiomata and severe varicose veins. Pulsation in the veins, a thrill and a bruit are definite proof of arterio-venous fistulae, but /

but their absence by no means rules out the diagnosis. There is an increased temperature, the Nicoladoni bradycardia reaction is positive and other cardio-vascular effects may be produced, culminating in congestive heart failure. A deficient circulation to the distal part of the limb is frequent in the more advanced lesions, as shown by chronic indolent ulcers and the onset of gangrene. In the neck, similar features are present, though hypertrophy of the jaws and skull on one side is not common. The patient may, however, be more distressed by buzzing, throbbing, attacks of dizziness and faintness. In all situations, there is a high oxygen content of the venous blood and arteriography may show up one or more fistulae.

Haemangiomata of varying descriptions have also been designated as the diagnosis of cases showing the features of any of the types of lesion just described. They are certainly a most ill-defined group, including perhaps true angiomatous tumours and also lesions which definitely are not tumours. The subject is discussed more suitably in Section Seven.

In surveying the clinical features and diagnosis in the various degrees of congenital vascular anomalies, it is seen that particularly common features are the triad of osteohypertrophy, haemangiomata and varicose veins, and the various local and general circulatory changes. The same methods of examination are applicable and it has been shown desirable and advantageous to consider the different types of lesion as a whole. In addition, it will be demonstrated how the same complications may develop, such as bony abnormalities and nervous system disorders. In the past, it may be generally stated that, in the presence of pulsation in the veins, a thrill and a bruit, a cirsoid aneurysm was diagnosed in a localised lesion and an arterio-venous aneurysm in a more generalised lesion, and that, in the absence of these signs, the lesion was designated a venous angioma when localised and small, and phlebectasis when extensive. Among the reasons for the present day approach to the problem of these vascular anomalies, the most important appear to be the increased use of the estimation of the oxygen content of the venous blood, the development of arteriography, and new ideas on the pathology of a cirsoid aneurysm.

THE SIZE OF THE AFFECTED PART.

Variations in Size.

It is possible that no change in size is present. Hypertrophy of a limb, and less often of part /

part of the skull, jaws or trunk, is such an outstanding feature, occurring in a large proportion of cases, that much emphasis has been given to it. Haemangiectatic hypertrophy, a term coined by Parkes Weber, is conveniently applied to cases associated with vascular anomalies and haemangiomata, and is thus the type to be discussed here. Atrophy, however, is an alternative, though rare, finding and several variations of hypertrophy and atrophy are now enumerated, with chief reference to the limbs. The bones may be of quite normal structure, but pathological changes in bone, either localised or generalised throughout a limb, are by no means uncommon. Muscular hypertrophy may be considerable but there is seldom any increase in the strength of a limb.

A uniform hypertrophy of one complete limb, including the shoulder or pelvic girdle, is probably the most typical appearance, exemplified by Cases Three, Four and Eleven. All the tissues are involved in the overgrowth and the limb is of normal shape and well formed.

Hemihypertrophy is a term applied to hypertrophy of a large part of one side of the body. The upper and lower limbs alone may be involved, as described, for example, by Parkes Weber (116) or Ward, C.E. and Horton (98). In addition, one half of the skull and jaws may be affected, as reported by Finlayson (7), or one half of the thorax and abdomen or one half of the external genitalia.

Crossed hypertrophy, mentioned by Parkes Weber is very rare, and consists of hypertrophy of one upper limb and the opposite lower limb.

A patchy type of hypertrophy is recognised and may involve any number of limbs. In Case One, the forearms were enlarged in relation to the arms, one forearm was larger than the other and certain digits of both hands and feet showed an excessive degree of growth. Lee, W.E. and Freeman (89) also reported such a development.

Occasionally a limb may show an increase in length only, as mentioned by Horton (92), or an in crease in girth only.

Atrophy of a limb may occur to a varying degree instead of the more common hypertrophy. This atrophy may be quite uniform in character and the limb may appear quite normal in shape and well developed, as seen in references by Reid (76) and Veal and McCord (57)(Case 7). On the other hand, a limb may be shorter /

shorter but of increased girth, Stewart and Bettin (24) mentioning two examples. Finally, the limb may show a severe degree of stunting, with poor development of bone and muscle, but with apparent swelling due to enlarged veins, and associated with much loss of function. Such a finding may be a primary lesion, but is more often a secondary change resulting from intensive X-Ray or radium treatment, as in Cases Seven and Eight.

The skull, jaws and face may show similar variations in association with local vascular lesions or as part of widespread lesions as in hemihypertrophy. Hypertrophy of the bone and soft tissues was described by Duzea and by Barwell, both quoted by Klippel and Trenaunay (11). On the other hand, Case Six showed severe atrophy of the jaws but gross hyperplasia of the soft tissues, and Case Twelve hypertrophy of the auricular cartilage and the soft tissues.

Other Causes of Localised Overgrowth.

Several other conditions are known to give rise to hypertrophy of one limb or one side of the body, and require to be mentioned as possible sources of confusion in the diagnosis of congenital haemangiectatic hypertrophy. Only the important causes are included.

Congenital hypertrophy has been described by Wakefield and Hines (46b) as a chaotic bizarre syndrome, with increase in size of the affected parts but without increased strength and for which no satisfactory explanation has been given. The appearances of this condition resemble those of haemangiectatic hypertrophy, except for the absence of a vascular lesion. Wakefield and Hines described six such cases and Peabody (58) described four. Among other references are those of Bankart (194) and Hutchison (195).

Localised gigantism, believed to be due to a pituitary dysfunction, may produce irregular types of hypertrophy. Case One was at one time believed to be an example, but the presence of vascular abnormalities tended to exclude the possibility. Whether due to a definite pituitary disorder or not, a monstrous localised form of hypertrophy of one or two digits has been described by Parkes Weber (116) and an excellent illustration has been given by Gould and Pyle (123b) of a tremendous overgrowth of the third finger. Chandler (62) also illustrated examples of local overgrowth of the hands and feet, without any vascular anomaly.

Neurofibromatosis very rarely gives rise to a congenital hypertrophy of a limb, but Campbell (193) reported such a case. The disease is, however, a well recognised /

recognised cause of elephantiasis occurring at a later age.

A lymphatic abnormality, either a congenital lymphangioma or congenital lymphoedema, may occur as a solitary lesion or may be associated with blood vascular abnormalities. The subject will be discussed separately.

Hypertrophy of a limb may be produced as a result of a local congestive condition at the period of growth and, at a subsequent date, it may be difficult to distinguish it from a true congenital abnormality. Such causes are osteomyelitis, syphilis of bone and tuberculosis of a joint causing stimulation of a neighbouring epiphyseal cartilage. Causes of acquired elephantiasis, such as all types of venous or lymphatic obstructions, and tumours of the soft tissues, scarcely come into this category.

Occasionally, it may be difficult to decide whether the larger or the smaller limb is the abnormal one, and in fact, in Case Four, the smaller limb had once been considered the one deformed. The most common causes of shortening of a limb are infantile paralysis, congenital bony dysplasias, destructive bone and joint infections, bone tumours, bone injuries, and hemiatrophy of unknown etiology.

THE APPEARANCE OF THE HAEMANGIOMATA.

Capillary Haemangiomata.

The capillary, cutaneous haemangioma is probably the commonest skin lesion, but varies greatly in size. It may be quite small, a mere fraction of an inch in diameter, and isolated, or it may be extensive and unbroken, and cover a large area of the body surface. It may have a patchy distribution where several separate lesions are situated in the same region.

The exact distribution of the angiomata is variable but there may be very precise boundaries. It has been claimed, for example by Fitzwilliams (179), that the extension and growth of a naevus are intimately connected with the nerve supply of a part; this may be demonstrated in any situation. When occurring on the face, intracranial changes may co-exist, the association of lesions then being known as the Sturge-Weber disease, which will be described subsequently. From a study of my own series of cases, there was no satisfactory proof of any true nerve distribution of the /

the lesions. In Case One, the mid line formed a rigid line of division between the lesions on the two sides, and in Cases Three and Four, the angiomata were almost entirely confined to the limits of a limb. On the other hand, in Cases Six and Seven, the lesions in the face and neck, which were mixed capillary and cavernous, were quite irregular in their distribution.

The typical capillary haemangioma is flat and perhaps slightly raised up from the surrounding healthy skin. It is frequently associated with a cavernous haemangioma and with venous varicosities. The colour varies considerably from a very pale pink to a dusky cyanosis, and may become more intense on congestion of the part. Blanching on pressure is common. A brownish pigmentation is rarely present, but is not a feature necessarily due to the actual angioma. The lesion is most often noted at birth or soon after. Subsequently it may disappear completely or after a few years it may spread widely.

Telangiectases.

Telangiectases occur in the skin and mucous membranes, may be single or multiple, but form a wide, rather ill-defined group. They take the form of small red or blue spots or streaks, a few millimetres in diameter. Most are quite painless, the exception being the type due to a glomangioma. Haemorrhage is common after an injury.

The type of telangiectases chiefly to be considered here in that associated with other vascular lesions, such as arterio-venous fistulae and haemangiomata. It is usually present at birth or becomes apparent soon after. Blue telangiectatic spots were present in several of my cases and were soft and easily compressible. In Case Two in the lower limb, in Case Six in the face and neck, in Case Seven in the upper limb, face and neck, and in Case Eight in the upper limb, they were present along with gross venous varicosities, but in Case Eight, there was in addition an isolated lesion on the nose. These all looked merely like small localised dilatations of superficial veins, though by some they might be considered small cavernous haemangiomata. A red telangiectatic spot is sometimes the first obvious sign of extensive arterio-venous fistulae and examples of such a development are seen in the Cases of Müller, quoted by Bland Sutton (127), Bernheim (25) and Wilbur (39).

On the shoulder regions in Cases Seven and Eight /

Eight, there were also numerous red telangiectatic spots of a different nature from the above but there was little doubt that they were the sequel of intensive X-Ray treatment. This is a point of importance in connection with X-Ray treatment, as it may produce as disfiguring an appearance as the original lesion.

A glomangioma, often present at birth, is a cause of a telangiectasis, as was well illustrated in Case Nine. The clinical appearances, however, were in no way different from the blue telangiectases already mentioned. This subject will be dealt with fully in a later section.

The common de Morgan's spots are seen as minute red spots on the chest and abdominal wall and form a type of telangiectases. They occur in adult life, are of unknown etiology and appear to be unrelated to other types.

A very rare cause of telangiectases is the condition known as Rendu-Osler-Weber disease, which is characterised by multiple hereditary telangiectases of the skin and mucous membranes. Though it is believed to be due to a congenital defect, it occurs in middle life. It takes the form of minute red or blue spots or streaks, which are liable to bleed, epistaxis being particularly common. Reference to the disease has been made by Parkes Weber (115) and Harvey, Dawson and Innes (147).

Other acquired causes of telangiectases, such as the venous dilatations of the nose in hepatic disease, do not require consideration here, as they are not liable to be confused with the congenital conditions.

Cavernous Haemangiomata.

This type of lesion has often been described in connection with vascular anomalies, but it is rather an indefinite entity. On the one hand it may be an extension of a capillary haemangioma, and on the other hand it may take the form of venous dilatations, indistinguishable from varicose veins. Of variable size, the lesion is soft and easily compressible, rather nodular and blue or red on the surface. Case Six of my series was an example of what is generally believed to be an extensive cavernous haemangioma, though in my opinion it was more likely to be a developmental anomaly rather than a true tumour.

THE VARICOSE VEINS.

Variations in the Appearance.

In the lower limb, the appearances may be the same as in ordinary varicose veins, and in fact many cases of arterio-venous fistulae have at first been mistaken for the common condition. A grossly dilated long saphenous vein may stretch between the foot and the groin, and have complete incompetence of the valves, as shown by the Trendelenburg test. In the thigh, such a vein may or may not be straight, but below the knee it becomes tortuous and convoluted. In places there may be only a thin covering of atrophic skin, so that severe haemorrhage is likely.

An alternative finding is an enlarged varicose vein on the lateral side of the leg and thigh, which at its upper end passes deeply into the buttock to communicate with gluteal veins. Such a vein was present in the right lower limb of Case One and in Case Three, and references to similar cases have been made by Lee, W.E. and Freeman (89) and by De Takats (51). The long saphenous vein was normal in all these examples.

Another type of varicose dilatation of the veins has often been mistakenly called haemangioma. In this case, part of the head, neck or trunk or part or whole of a limb may be involved in a most extreme degree of dilatation of the veins, which form an enormous plexus with innumerable connections. The veins are usually situated both superficial and deep to the deep fascia, and they do not tend to follow the course of a single main vein, such as the long saphenous or cephalic. The overlying skin usually shows a blue discolouration or is the site of a capillary haemangioma. When the veins are very superficial, they may bulge through the attenuated skin to form prominent venous bullae. In the most severe cases, the venous plexuses extend into the muscles, replacing much of their bulk and transforming a limb into a soft compressible structure. On dependency, such a limb looks greatly swollen, but, on elevation, the blood tends to drain out of the veins, causing a definite reduction in circumference. The possible involvement of the nerve trunks and bones will be discussed later. Amongst my own series, Cases Two, Six, Seven and Eight showed the above widespread type of venous dilatations.

Though a most unusual feature, a glomangioma may produce the appearances of a collection of varicose veins, illustrations being mentioned in the report on Case Nine.

Phlebitis /

Phlebitis.

Phlebitis is a common cause of pain in congenital vascular anomalies. It is usually of a mild non-infective character, produces thrombosis in the veins, with tenderness and swelling of the part, and is followed by obliteration of the lumen of the vein. Edwards and Edwards (181) have shown that such a vein may recanalise later, but that the valves become irreparably damaged. Thus spread of the varicosities may result, and Lee, W.E. and Freeman (89) showed, in Case One of their series, how symptoms only became severe after an attack of phlebitis. This sequel is not constant, as thrombosis may tend to natural arrest of the lesion, particularly if no extensive arteriovenous communications are present.

Less often the phlebitis is of an acute, highly infective type, as was found in Case Eight of my series. A haemolytic streptococcus was the causative organism, giving rise to localised abscesses eventually, and also producing a state of pyaemia by detachment of septic emboli.

Phleboliths.

Phleboliths appear to reach their maximum development in cases of vascular anomaly and angiomata. In a normal individual they are quite symptomless and are an accidental finding on X-Ray examination of the pelvis. In my own series, they were a most prominent feature in four cases and they have been recognised in such cases for many years. In these cases, the majority of the phleboliths are symptomless, but palpation reveals their presence as hard, mobile nodules in the subcutaneous tissues. They may, however, be quite tender to the touch, especially if in a situation exposed to numerous minor traumata, for example in Case Seven at the angle of the mandible and in Case Eight at the wrist. This latter example eventually demonstrated the unusual phenomenon of spontaneous extrusion of the phlebolith.

In tracing the evolution of a phlebolith, it appears that thrombosis first takes place in the veins due to stagnation of blood flow or phlebitis. The resulting thrombus becomes fibrosed and later calcified, forming the typical round nodule evident on X-Ray examination. The phlebolith may later increase in size by the deposition of layers of calcium and ultimately may become more than $\frac{1}{2}$ inch in diameter.

In 1921, Wakeley (19) commented on the extreme rarity of calcification in angiomata, quoting two personal cases and indicating only one previous reference /

reference. He was, however, considerably misled, as many examples had been published before that date, for example Duncan (10) in 1900 and Davis (13a) in 1908.

THE STATE OF THE LOCAL CIRCULATION.

Possible Variations.

Apart from varicosities, there may be a complete absence of any circulatory changes in the affected part, but, on the other hand, many varied effects may be produced in the several types of lesion. Dilation of the arteries, pulsation in the veins, a palpable thrill and an audible bruit are definite evidence of arterio-venous fistulae, but their absence does not rule out the diagnosis. An increase in the local temperature, haemorrhage and a rise in the local blood pressure are common but inconstant features. Signs of vascular insufficiency are variable in their appearance and they may develop with little warning in a previously quiescent case.

Dilatation of the Arteries.

In true phlebectasis and in the less prominent degrees of arterio-venous fistulae, this feature is absent.

In the case of one or more fistulae involving a large artery such as the femoral, the axillary or a carotid, considerable dilatation may take place proximal to the fistulae. The artery beyond that level is almost always contracted, but rarely may be dilated. The dilated artery may be twice or three times the normal size, a fact evident on palpation or inspection of its excessive pulsations. Sometimes the dilatation may be extreme but localised so that a fusiform aneurysm forms. At other times, the dilated artery becomes unduly tortuous and actually lengthened. A rare complication, reported by Homans (86), is spontaneous rupture of the thin-walled dilated artery.

In a typical localised cirsoid aneurysm, the dilatation involves one or several arteries leading towards it.

Abnormal Pulsation in the Veins.

This is positive evidence of arterio-venous fistulae, but is often absent. It is generally believed now that the pulsatile vessels in a cirsoid aneurysm are veins, not arteries as formerly understood. In all cases both superficial and deep veins may /

may be affected, though the pulsation is more obvious and striking in the former so that the affected part becomes transformed into a pulsating mass of writhing distended vessels. The pulsation is caused by arterial blood entering veins directly from arteries, the higher pressure and systolic pulsation thus being transmitted. The intensity of the pulsation varies according to the size of the fistulae, and the veins at the site of the fistulae, or distal or proximal to them, become involved.

A Palpable Thrill and an Audible Bruit.

These outstanding features are usually found only in the advanced stages, where there is dilatation of the arteries and where one or more large arterio-venous fistulae are present. They may be absent when the fistulae are small and multiple.

The proximal dilatation of a main artery, sometimes amounting to a fusiform aneurysmal dilatation, itself may produce a thrill and a bruit which tend to be systolic and may be soft and blowing or loud and harsh. In addition, the passage of blood from an artery to a vein through a fistula gives rise to a thrill and a bruit which may be continuous and accentuated during systole or may be purely systolic.

The propagation of a bruit varies. The bruit may be audible only in the region of a fistula or a considerable distance distal to it. In the case of fistulae in the distal part of a limb, the bruit may be made out in one of the large proximal arteries. In a typical cirsoid aneurysm of the scalp, the thrill and bruit are demonstrable over the whole affected area as well as over the proximal arteries. The thrill and bruit may be made out over an entire limb in relation to the large pulsatile veins of a severe case of arterio-venous fistulae.

A thrill and a bruit have been described by many authors. They were present over the large vessels in the foot in Case Five and over the iliac and femoral vessels in Case Four, and they were very marked in Case Twelve.

A Collateral Circulation.

In cases where much arterial blood is shunted directly into the veins, a satisfactory collateral circulation usually develops, thus maintaining adequate nutrition to the parts beyond. This fact was pointed out by Reid (74), though it is more evident in traumatic cases. Ultimately such a circulation may fail and signs of vascular insufficiency then develop.

The /

The Temperature of the Affected Part.

Congenital vascular anomalies of all types tend to be associated with a localised increase of temperature. In cases of definite arterio-venous fistulae, the temperature around that site may be increased, with a decrease in the parts beyond, but on the other hand, a whole limb may show the increase. In phlebectasis, a whole limb may similarly have an increased temperature. Such changes may be obvious to the palpating hand, but are better tested by a special skin thermometer.

Haemorrhage.

Spontaneous bleeding may follow the rupture of a telangiectatic spot or a superficial dilated vein, or it may take place from an ulcer. Bleeding may be due to injury, as, for example, by a razor. In cases of phlebectasis, it was noted that mild bleeding persisted for several weeks after operation.

The Arterial Blood Pressure in a Limb.

This may be raised in cases of arterio-venous fistulae but it is not a constant nor an important feature. In Case Four, for example, the blood pressure in the affected limb was 152/92, whereas the general blood pressure, as measured in the other limbs was 122/82.

THE SIGNS OF AN INCOMPETENT CIRCULATION.

Occurrence.

Varying signs may be produced by an incompetent circulation and will be discussed more fully in the section on pathology. They may occur in cases of pure phlebectasis and in arterio-venous fistulae, and will be discussed with chief reference to the limbs, being more obvious there. A lesion involving the carotid arteries and jugular veins may give rise to cerebral signs, such as fainting, due to a transient poor blood supply and less often hemiplegia, due to a more permanent impairment or to an embolus. A cirsoid aneurysm of the scalp may develop ulceration on the surface as a result of gradual attenuation of the skin.

In arterio-venous fistulae, especially in the limbs, it seems paradoxical that signs of vascular insufficiency can develop in spite of the apparent great increase in the amount of blood entering the part. The explanation is that so much blood is short /

short-circuited from the arteries into the veins that the parts beyond actually suffer from a decreased supply of arterial blood.

Cyanosis and Oedema.

These signs are amongst the earliest signs of vascular insufficiency and impending gangrene in the hands and feet in cases of arterio-venous fistulae. They may, however, be of less significance in phlebectasis, where the cyanosis is merely the result of the filling of varicose veins and large angiomata by venous blood.

Ulceration.

Ulcers may be found in any situation, but most often in the fingers, toes and legs, and in stumps following amputation for gangrene. Usually precipitated by a trivial injury and superadded infection, the ulcer tends to be very indolent, chronic and painful, and though it may heal temporarily with rest, it tends to break down again sooner or later. The surrounding skin is often hot, shiny, red and oedematous, and haemorrhage from the ulcer may be severe.

In pure phlebectasis, the significance of an ulcer of the leg may be no greater than that of the common varicose ulcer. It is due to stasis in the veins and congestion in the perivascular tissues and may be followed by brown pigmentation of the surrounding skin.

Ulceration of the digits, and less often the hands, feet or legs, occurring in arterio-venous aneurysms, is of ill omen, as being a common presage of gangrene. It is definitely due to a deficient supply of arterial blood to the affected part, caused by the loss of blood through the fistulae. Brown cutaneous pigmentation again may be present.

Ulceration of an amputation stump may occur as a result of new fistulae becoming patent in the proximal part of a limb, and is an indication for amputation at a higher level.

Intermittent Claudication.

This is not common. It may be noted, in the lower limb especially, as a sign of impending vascular insufficiency. So much arterial blood is lost through fistulae into the veins that the main artery carries a deficient amount of blood, and in addition the collateral circulation begins to fail. The distal pulses in the /

the limb are feeble or absent.

Gangrene.

Gangrene in a limb is a complication of arterio-venous fistulae and is usually preceded by some of the above signs. It may be well localised to the digits or may spread to the hands or feet. Though at times of a dry type, it may on the other hand be of a moist and infective type when venous engorgement is marked. A rare type of gangrene is produced by the lodgment of an embolus derived from an aneurysm of a main artery proximal to arterio-venous fistulae, such a case being described by Wilbur (39). Another cause of gangrene of a limb, often affecting a large part of it, is an ill-advised operation for ligation of a main artery proximal to arterio-venous fistulae; this will be discussed in detail later.

GENERAL CARDIO-VASCULAR EFFECTS.

Occurrence.

These interesting and varied phenomena are well known in traumatic arterio-venous fistulae, but they are seldom so constant or extreme in congenital vascular anomalies. Nevertheless, certain features are found in phlebectasis, in a localised cirsoid aneurysm and in an extensive arterio-venous aneurysm. Several variations are possible.

Changes in Phlebectasis.

In true phlebectasis of the lower limb, Lee, W.E. and Freeman (89) have pointed out how, on the assumption of the erect position from the recumbent, a large quantity of blood flows suddenly into the dilated varicose veins and the angiomata, and becomes temporarily lost from the general circulation. The result is an immediate increase in the pulse rate, a rise in the diastolic and a fall in the systolic blood pressure, all of which were suggested to be comparable to the physiological effects of haemorrhage. As the return of blood to the right side of the heart diminishes, there is a compensatory increase in pulse rate with vasoconstriction, and the pulse pressure decreases both by a decrease in the systolic and an increase in the diastolic blood pressures. Compensation for the impaired cardiac return is accomplished by these protective mechanisms. When the loss of circulatory blood is too great, the cerebral tissues become anoxemic and fainting occurs.

Similar /

Similar changes were elicited in Cases One & Ten They might also be found in some cases of arterio-venous fistulae.

The Nicoladoni or Branham or Isreel Bradycardia Phenomenon.

Matas (36a) stated that the Branham syndrome is manifested on compression or obliteration of a traumatic arterio-venous fistula, and the Nicoladoni-Israel phenomenon in congenital arterio-venous angioma. Most authorities, however, do not attempt this particular differentiation and apply the same names to both traumatic and congenital cases. Nicoladoni in 1875 and Israel independently in 1877 described the test in cases of congenital arterio-venous fistulae involving the upper and lower limbs respectively; Branham, often credited as the first observer, described it in 1890 in connection with a traumatic case. It is only in its relationship to congenital cases that the phenomenon is here discussed though it is much more common in traumatic cases and is difficult to elicit in congenital cases owing to multiple fistulae.

The test is simply carried out by exerting digital pressure on a main artery over or proximal to the arterio-venous fistulae, so as to obliterate the flow of blood along the artery and into the fistulae. The result is an immediate slowing of the pulse rate, which may vary from as little as five to as many as forty beats per minute. The reaction is directly related to the seriousness of any cardiac damage, to the size of the fistulae and to the amount of blood passing through the fistulae. Thus, if the fistulae are small, the phenomenon may not be observed; the larger the fistulae, the more marked is the change in pulse rate.

Various explanations have been advanced. Closure of the fistulae certainly produces a sudden rise in systolic and diastolic blood pressure, which however, is not permanent. Reid and McGuire (77) stated that this rise either reflexly or directly stimulates the cardio-inhibitory centre of the brain or possibly has a direct effect upon the myocardium. Lewis, Sir T. and Drury (122) stated that the fall in pulse rate is vagal in origin and is abolished by atropinisation. Pemberton J. and Saint (35) mentioned that the slowing of the heart rate is in accordance with Marey's law, that the pulse rate varies inversely as the blood pressure. The mechanism is that a rise in blood pressure, by stretching the wall of the aorta, stimulates the ending of the depressor nerve; as a result, the cardio-inhibitory centre is excited and impulses /

impulses by way of the vagi produce a reduction of the pulse rate.

A similar test is elicited on elevation of a limb; the amount of blood flowing through the fistulae is reduced and the pulse rate falls.

The Nicoladoni reaction was noted in Cases Four, Five, Seven and Eight of my own series.

Cardiac Enlargement.

This is a comparatively rare occurrence in congenital vascular anomalies, though it is common in traumatic arterio-venous fistula. Pemberton, J. and Saint (35) suggested that this fact is due to the better adaptability of the cardio-vascular mechanism when the abnormality exists from birth. It is recognised, in both congenital and traumatic cases, that signs, such as an elevation of the blood pressure and a slowing of the heart rate on closure of a fistula, are usually the first evidence of early cardiac damage. It is possible, however, especially in an adult, that the cardiac changes may be due to an independent cause. This point was raised in Case Six where cardiac enlargement was associated with hypertension but was assumed to be due to arterio-venous fistulae in the absence of any recognisable cause for the hypertension.

Much experimental work has been carried out on traumatic arterio-venous fistulae but some of the findings are not directly applicable to a congenital lesion. Lewis, Sir T. and Drury (122) believed that the cardiac enlargement is chiefly a dilatation and is due to a deficient nutrition of the heart muscle, consequent on a fall of mean arterial pressure and a diminished supply of oxygenated blood to the coronary vessels.

Holman (61) produced much evidence against the views of Lewis and Drury. Finding that the blood volume is greater than normal, and that the weight of an experimental animal's heart is increased, he proposed that cardiac hypertrophy takes place in order to propel forwards this greater amount of blood. He believed also that the dilatation of an artery proximal to a fistula spreads retrogradely to affect all the arterial bed between the heart and the fistula and that the heart shares gradually in this dilatation until ultimately both hypertrophy and dilatation are present.

Reid (74) failed to detect any cardiac changes /

changes whenever the artery proximal to the fistula had not been enlarged, and stated, also, that the degree of cardiac damage directly depended on the vessels involved and on the size of the fistula.

Whichever theory is correct, in a severe case complete cardiac decompensation takes place, with peripheral oedema, ascites, hydrothorax and extreme dilatation of the heart. The point of great importance, however, is that elimination of the peripheral arterio-venous fistula, either by closure or perhaps by amputation of a limb, results in a complete recovery by the heart of its normal size and function, even after years. Matas and Heninger (36b) used the term reversible heart to indicate this return to normal and stated that it only occurs in traumatic and congenital arterio-venous fistulae, in myxoedema and in beriberi, and in chronic pulmonary tuberculosis.

Among the recorded cases of congenital vascular anomalies, a few have shown definite cardiac enlargement. Holman (61) quoted Rosler in describing other instances in which cardiac enlargement was detected. Matas (36a) and Matas and Heninger (36b), in recording the same case, described the severe degree of dilatation of the heart, which recovered completely once the affected upper limb had been amputated. Rienhoff (22) mentioned considerable shortness of breath which improved after closure of arterio-venous fistulae in the neck, and Horton (92) reported the occurrence of cardiac hypertrophy among his patients. Steinberg, Grishman and Sussman (105), and Touroff (106) reported a progressive degree of heart failure, which was the chief indication for ligation of the first part of the left subclavian artery. Gangrene resulting, the limb was amputated and the condition of the heart at once improved. It is thus seen that the condition of the heart may occasionally be a deciding factor in the treatment of severe cases of arterio-venous fistulae.

SUBJECTIVE PHENOMENA.

Pain is a variable feature and is often absent. Phlebitis usually causes it, and a large phlebolith may be tender. Ulceration, impending gangrene and involvement of nerve trunks are also associated with pain, and trauma, even trivial, often accounts for its onset. Inequality of the lower limbs may cause a severe postural disturbance, so that chronic sacro-iliac arthritis and permanent scoliosis result. Arthritis, due to infection in and around joints, produces pain and painful joint contractures. Considerable loss of function is due to pain or to the abnormal size of a part.

Disfigurement /

Disfigurement, especially in a lesion of the face, may cause the patient much concern, and an increased growth of hair or brown pigmentation may be unsightly. The increased temperature of a part may be accurately noted by the patient, who complains of a feeling of heat and of excessive sweating.

The presence of a thrill, a bruit and pulsations in the veins, particularly in the head and neck, gives rise to most unpleasant, throbbing, painful sensations. A feeling of suffocation and difficulty in swallowing are serious features. They may be due to engorgement of varices of the larynx or pharynx, or to the external pressure of large vessels, and they may be precipitated by X-Ray or radium treatment or by electrolysis. Dyspnoea may also be a sign of cardiac failure.

S E C T I O N F I V E.

REVIEW of SPECIAL METHODS of EXAMINATION.

STRAIGHT X-RAY EXAMINATION.

Scope of the Examination.

X-Ray examination is to be recommended in every case, as it may give most valuable and unexpected information. In the case of a limb, the investigation should include the entire limb and also the opposite limb, and in the case of the neck, face or head, a complete examination of the whole region should be carried out, as intracranial changes may be found in addition to these more obvious. Both the bony and the soft tissues may give abnormal shadows, but in other cases no change in size or structure is to be ascertained. Several appearances are met with, and it is uncertain to what extent those in bone are produced by variations in blood supply, by vascular malformation or by tumour growth. Certain of these features will be discussed more suitably in Section Eight, and only the radiological findings will be mentioned here.

Variations in the Size of the Bones.

A sufficient account was given in Section Four of the possible variations in size which are quite evident on X-Ray examination. If the two upper or lower limbs are examined on the same film, an accurate idea is obtained of the differences in length and girth, as in Cases Three, Four & Eleven. Failure of development of the epiphysis may be apparent. The changes in size bear no particular relationship to those in structure, as seen, for example, in Case Three where the tibia was hypertrophied and of normal structure but the femur was hypertrophied and the site of a pathological change. In the presence of the extensive type of angioma of bone, there is usually atrophy of the bones, in girth if not in length.

Osteoporosis.

Osteoporosis occurs, in any situation, in bones of normal size and structure, or in bones of normal structure but atrophied, or in bones which also show structural changes. The associated vascular anomaly of the soft tissues appears to produce an excessive vascularity of the bones and thus osteoporosis. It is possible, however, that the disuse of an affected part may be a factor in the production of the osteoporosis, as was seen in the tarsal or metatarsal bones in Case Five and in the jaws in Case Six.

Angioma /

Angioma of Bone.

This is a lesion about which there is considerable dubiety as to its diagnosis and its exact nature, because the term does not necessarily signify an actual neoplasm. A solitary angioma of bone may be associated with a vascular anomaly of the soft tissues or it may occur in its absence. The term angioma is also applied to a widespread or multiple lesion which is always accompanied by a lesion of the soft parts. Radiologically, however, there appears to be no hard and fast line of distinction between osteoporosis, a solitary angioma and a widespread angioma, and it is possible that they all may be due to the same underlying cause.

The solitary angioma has been found in almost any bone, but Bucy and Capp (136), in a good account, classify it according to its occurrence in flat bones such as skull, scapula or pelvis, in the vertebrae and in the long or tubular bones. In the skull, the lesion shows as a local erosion with well defined margin, enclosing a meshwork of fine trabeculae which often radiate from the centre of the tumour to give the typical sunburst appearance; a recent report on such lesions was given by Rowbotham (132). In the vertebrae, chiefly the bodies, the appearance is that of a honeycombed rarefaction and vertical denser striations, followed by collapse and wedging.

In the long bones, with which the discussion is mainly concerned, the lesion is composed of small loculations with an interspersed, fine, fibrillary network, sometimes called a soap bubble or sunburst appearance; the cortex is usually destroyed but the periosteum remains intact, though expanded. Sometimes it may be impossible to distinguish such a condition from a giant cell tumour. Though certain of such isolated angiomata of bone may be actual neoplasms, the findings in two cases of my series were definitely against such a view. In Case Three and Case Five, the lesion in bone was intimately associated with arterio-venous fistulae, suggesting that enlarged vascular channels and sinuses occupied the affected portion of bone.

In comparison to the above single lesions, the extensive type of angioma involves the whole extent of one bone or even many bones in the one limb. In general, there is rarefaction of an irregular type, producing a honeycombed appearance or one resembling multiple small cysts. There is usually an associated atrophy of bone. It is believed that enlarged vascular channels in the bone are the cause of the abnormal appearance. Cases Two, Seven and /

and Eight illustrated such extensive lesions.

Pathological Fracture.

This complication is easily recognised. Non union may occur.

Soft Tissue Outlines.

The increased size of the soft tissues, as well as of the bone, may be evident as in Cases Three and Four, or there may be a considerable soft tissue swelling associated with atrophied bones as in Cases Two and Six.

On the other hand, as in Cases Seven and Eight, there may be atrophy of the muscle and obliteration of the normal muscle lines due to its replacement by the abnormal vascular development; the cutaneous outline may then be irregular and nodular due to the large distended superficial veins.

Calcification of blood vessels is rare, and has been described in connection with traumatic arterio-venous fistulae, but not congenital.

Phleboliths.

Phleboliths produce a most outstanding and uncommon picture. They tend to be scattered diffusely about the affected part, such as a whole limb or the neck, and they vary in size from a mere pin point to more than half an inch in diameter. The small ones are of uniform density, but the large ones show signs of their increase in size by the laying down of calcium in concentric rings. The outline of a phlebolith is smooth and round and there is seldom any difficulty in the diagnosis. Calcified tuberculous glands, the most likely cause of confusion, are not of a uniform density and are irregular in outline. Calcified cysticercus cysts must also be ruled out.

Cranial and Intracranial Changes.

Mention is made of these only in connection with their association with more widespread vascular abnormalities. The angioma of the skull has already been discussed. X-Ray examination of the skull may show increased vascular markings, due to enlargement of meningeal vessels or diploic veins, which may or may not be associated with a vascular lesion, such as a cirsoid aneurysm, in the scalp overlying. Abnormal perforation of the skull by a particularly large venous channel may be apparent. Cases Seven and Eight illustrated these changes to a slight degree.

In the Sturge-Weber disease, a facial haemangioma is associated with a similar lesion of the leptomeninges. X-Ray examination may show calcareous deposits in the latter site.

ANGIOGRAPHY.

History.

The history of its use in connection with arterio-venous fistulae only is mentioned here, as its use in other circumstances is beyond the scope of the discussion. Dealing with a case of traumatic arterio-venous fistula of the femoral vessels, Horton, in 1935, was the first to use the method of arteriography to demonstrate the exact site of the fistula. In 1935, Horton and Ghormley (95) claimed to be the first to use the method in congenital arterio-venous fistulae, though, as already mentioned, it was used in Case Five of my series in the same year. These authors strongly recommended arteriography in all cases of arterio-venous fistulae before treatment is carried out, as only by such means can an accurate diagnosis be made of the level of the lesion; since using it regularly, the number of amputations became greatly reduced. Allen E.V. and Camp (184) believed that the procedure is not of great diagnostic value in arterio-venous fistulae but that it is of importance in determining accurately the site of the fistulae.

Thorotrast.

There has been much controversy about the use of this substance for arteriography, some praising it as the best available, and others condemning it for its dangers. Thorotrast is the name applied to a stabilised solution of colloidal thorium dioxide sol, which consists of 19-20 % by weight of thorium dioxide. Allen E.V. and Camp (184) were of the opinion that the ideal substance is one which can be injected into an artery without producing pain, or immediate or delayed toxic effects, and which is of good radio-opacity in spite of dilution by blood after injection. They were enthusiastic advocates of thorotrast and believed it to be nearer the ideal than any other preparation except for the possible toxic effects. Veal and McCord (57) and Horton and Ghormley (95) used it for preference and considered it simple, efficacious and safe, provided the dosage is not much more than 10 c.c.

Its possible dangers, however, are such that the majority of authorities condemn its use. The American Medical Association (185)(186) made very full investigations into the use of thorotrast and recommended /

recommended that it be not accepted for injection into the blood stream. Their findings were of great interest and importance. It was conceded that it can be admitted into the body cavities and into the blood stream, with little deleterious effect, but it is picked up by the cells of the reticulo-endothelial system, especially in the liver and spleen, where it remains indefinitely. Its great risk is its radio-activity, as the degradation products of thorium emit alpha rays more penetrating than those of the radium series, and 10,000 times as toxic as the gamma rays used therapeutically. It is possible that as much as ten or fifteen years may elapse between its administration and the onset of gross tissue changes, such as necrosis or malignant disease, and no complacency may be permitted merely because of the absence of effects for a year or two. It is not advisable for use in arterio-venous fistulae or other vascular disorders of the limbs, in which there is no immediate threat to life or even average health, but it is justifiable to use for cerebral arteriography, particularly in cases of tumour, where the prognosis as to life is limited. Fleming and Chase (190) similarly considered its use dangerous where the expectancy of life is more than two years.

These two authors also drew attention to its non-specific mechanical effect of a foreign body. In the case reported by Matas (36a), thorotrast injected in the axilla and chest wall was still visible on X-Ray examination four years later and gave rise to tenderness over it. Matas suggested that the obliteration of the angioma at this site might possibly have been due to the separate or combined effects of X-Ray treatment and thorotrast.

Alternative Substances.

Various preparations have been used at different times and have been discussed in detail by Edwards, E.A. (182), Allen and Camp (184), and Bird (187). Among those which have fallen into disuse are the iodides and bromides of sodium, strontium, potassium and calcium; proteinated silver salts; bismuth in oil; and iodised oil and emulsified iodised oil. The most used of these was probably sodium iodide, 20 c.c of a 20% solution, which is irritating, though otherwise good.

At the present time, the preparations used for excretion urography are found to be satisfactory. They are non-toxic in the doses used, are quickly excreted from the body, do not damage the intima of vessels and are reputed not to cause pain on intravascular injection. This last fact is not always true /

true, as in Cases Seven, Eight and Nine definite cramp-like pain was produced and lasted for a few minutes. It is admitted that the density of these alternative preparations containing iodine is not so striking as that of thortrast, but visualisation of the vessels is quite satisfactory. One commonly used preparation is Uroselectan B or Pyelectan, which is the disodium salt of N-methyl-3:5 diiodo-4-pyridone 2:6-dicarboxylic acid. A more recent preparation is Diodrast or Per-Abrodil, which is 3:4 diiodo-4-pyridine-N-acetic acid diethanolamine and is available in aqueous solutions of 30-70%.

Technique of Arteriography.

Operative exposure of the artery to be injected may be carried out, a local anaesthetic often being satisfactory. The artery having been exposed, it has been usual to dissect it up and to strip it from its surroundings. A tape or a rubber tube, passed deep to it, can then be used for retraction and for temporary occlusion of the blood flow. The needle, attached to the syringe, is inserted obliquely through the wall of the artery into the lumen. The injection of the opaque medium is made quickly, and the blood allowed to flow in the artery. One or more exposures to X-Rays are then made of the part of the artery to be examined. The opening in the artery closes spontaneously on withdrawal of the needle, and the wound is closed. Recently Professor Learmonth (223) has recommended that the artery should not be dissected from its bed, in order to avoid spasm or damage to the collateral vessels.

A different technique, described by Allen and Camp (184) and used by other authorities, consists of a blind puncture of the artery, without any skin incision. In the case of the upper limb, the outstretched supinated position is used and a sphygmomanometer cuff is applied as near the shoulder as possible. A local anaesthetic is injected into the tissues overlying the lower part of the brachial artery, which is then entered with a venu-puncture needle attached to the syringe containing the radio-opaque material. As soon as bright red blood pulses forcibly into the syringe, the cuff is rapidly inflated above the systolic blood pressure and the injection is made. The needle is then quickly withdrawn, and, as pressure is made over the point of puncture to prevent leakage, the first X-Ray film is taken. The cuff is now quickly deflated to the level of the diastolic blood pressure for a period of two to four pulse beats, to permit the injected material to be carried more distally. The cuff is then quickly re-inflated to its previous pressure and a second film is taken. The procedure is repeated for a third film.

In /

In the case of the lower limb, after injection of a local anaesthetic, the femoral artery is punctured in the same manner just distal to the inguinal ligament. Pressure by an assistant's fingers over the artery replaces the sphygmomanometer cuff and the method otherwise is the same.

Difficulties of Arteriography.

The technique is exacting and calls for much practice and co-operation between the operator, the assistant and the radiologist. The radio-opaque solution is rapidly swept away by the blood stream and adequate visualisation depends on exposure of the film at the exact moment. If too much is injected, both arteries and veins are visualised, and, if too little, the terminal parts will not be clearly shown. If the exposure is too late, the veins alone will be shown.

During the injection, the patient may complain of pain, and later, if leakage has taken place, soreness and redness may persist around the site of injection.

Interpretation of Arteriogram.

A normal arteriogram is characterised by a smooth, uninterrupted contour of the lumens of the injected arteries, a direct course of these vessels, and the presence of no more than a minimum of collateral circulation.

An arteriogram in a case of arterio-venous fistula shows the following features, as noted by Allen and Camp (184) and Horton and Ghormley (94):- dilatation of the arteries leading to the fistula, absence of normal filling of the arteries distal to the fistula, and rapid filling of the veins or pooling near the fistula.

The arteriographic appearances were classified in more detail by Veal and McCord (57) and included:- a multiple type of communication, designated as arteriolar-venous, involving small superficial vessels and akin to a port wine birthmark; a single anastomosis between a large artery and a large vein, and also a communication of the veins with a large varicosity; a communication between a normal digital artery and normal veins by way of small arterioles or vascular pockets; or an angiomatous, or vascular tumour type of communication, the digital artery giving rise to small tufts of small arterioles.

Venography.

This investigation may be of value, but at

times it may give no more information than careful clinical examination. The veins may be visualised in two ways.

The method described by Allen and Camp for arteriography is carried out, but the films are taken later than those required to visualise the arteries.

The direct injection of an opaque medium into the veins gives an efficient visualisation, especially in marked varicose veins, an account of the method being given by Edwards (182). Tourniquets may be applied to isolate a desired segment of a vein to see its connections, or else a limb may be elevated, horizontal or dependent for the purpose of determination of the direction of the blood flow. Lee and Freeman (89) showed good visualisation of a large vein which communicated with a large venous lake in the buttock.

Results of Angiography in Personal Cases.

In Case Three, the femoral artery was injected with Perabrodil 35%. Visualisation of the vessels was satisfactory, but no definite pathological lesion was demonstrated, the only abnormal feature being rapid filling of the popliteal vein, without corresponding filling of the tibial veins. A fairly indirect communication between the popliteal artery and vein was thus suggested, shown subsequently to be chiefly, if not entirely, in the interior of the bone. Perabrodil 50% was similarly used in Case Eleven, with a negative result.

In Case Five, two arteriograms were made, the first by exposing the anterior tibial artery and the second the femoral artery. The Thorotrast gave an excellent shadow and visualised the vessels of the foot and toes accurately. The dosage was small and its use had certainly given rise to no toxic effects eight years later. The important findings were arterio-venous fistulae in the region of the second toe, the poor blood supply to the other toes, and the exceptional vascularity and dilatation of the vessels in the rest of the foot.

In Case Nine, the radial artery was injected with Pyelectan, giving satisfactory visualisation of the small arteries leading into the collection of veins which formed the lesion. Moderate cramp-like pain was caused by the injection, although otherwise the local anaesthesia acted perfectly.

In Cases Seven and Eight, Perabrodil 35% was used for venography, being injected into prominent superficial veins, and in Case Ten, Pyelectan was injected into the long saphenous vein. Several large veins were visualised but no satisfactory information was obtained.

From /

From a survey of personal and other cases, it seems that arteriography may vary in its ability to give information. It is probably most useful in cases where the diagnosis has already been made but where the site of arterio-venous fistulae has not been determined. It is most unlikely to give a positive result in doubtful cases where the oxygen content of the venous blood is normal, and, on the other hand, in the most obvious cases, the other simpler methods may be sufficient to make an accurate diagnosis. Certain technical difficulties may prevent the use of the investigation, such as arterio-venous fistulae in the pelvis or at the root of the neck, and excessive vascularity of the soft tissues overlying the artery. It was noted that Thorotrast gave a denser shadow than Perabrodil 35% or Pyelectan.

Venography by direct injection into a vein, does not appear to be an adequate substitute for arteriography in cases of arterio-venous fistulae, as, owing to the great capacity of the veins, the opaque medium is unable to visualise more than a small extent of them. It is more likely to be effective in a case of varicosity of a single large venous trunk, where its deeper ramifications can be visualised, as, for example, in the case of Lee and Freeman (89).

Visualisation of Haemangiomata.

Visualisation of capillary haemangiomata by the injection of a radio-opaque medium into an afferent artery may prove of value in determining more details about the exact nature of these lesions, and it is a method which will probably receive more investigation in the future. Pomeranz and Tunick (188) described the use of angiography in angiomata, but from their description it seems probable that the cases were not true tumours but were either congenital anomalies or acquired varicosities, giving rise to cavernous swellings. In addition to the diagnostic value of the procedure, they found that satisfactory obliteration of the vessels of the swellings took place after the injection of a radio-opaque solution.

Angio-Cardiography.

A method of visualisation of the chambers of the heart, the pulmonary circulation and the great blood vessels was described by Robb and Steinberg (189) in 1938. It was later carried to a further stage by Steinberg, Grishman and Sussmann (105), and was applied to cases of arterio-venous fistula, where direct injection into an artery was unsuitable or technically difficult. It consisted of the rapid introduction of two /

two injections of 30 c.c of Diodrast 70% into the antecubital vein, making several roentgen exposures, which could be recorded fluorographically or roentgenographically. In the case reported by these authors, it was possible to diagnose that the site of arteriovenous fistulae was in the region of the third part of the subclavian artery. From their use of angiocardiography for various conditions, they found it not entirely free from unpleasant effects. A fall in blood pressure was common and a few cases of urticaria and angioneurotic oedema occurred.

It seems that this method may find greater application in the future in order to determine the sites of arterio-venous fistulae involving the common carotid, the subclavian and the iliac arteries. The radiographical technique, however, is one of considerable difficulty, requiring several exposures at very short intervals and very accurately timed, as the flow of blood in the arteries is so rapid. Visualisation is also difficult on account of the great dilution of the opaque medium.

The method was not attempted in my personal cases, largely on account of the difficulties and uncertainties. It might have been of considerable value in Cases Four, Six, Seven and Eight, where arteriography was not possible.

OXYGEN CONTENT OF THE VENOUS BLOOD.

History.

The estimation of the oxygen content of blood in the regional veins is of the utmost value in the investigation, diagnosis and treatment of congenital vascular anomalies. The simplest test is non-quantitative and consists merely in the comparison of the colour of samples of blood from a vein in the affected part and from one in a normal part. Quite a definite difference may be appreciable in arteriovenous fistulae, as the more highly oxygenated blood from the affected part is bright red and the normal venous blood the usual dark bluish red. This colour change has long been known, for example, Warren in 1858 noted that arterial blood circulated in the veins of a varicose aneurysm. This method, however, was obviously inaccurate in that minor variations could not be determined.

The modern accurate quantitative test was probably described for the first time in 1927 by Brown (121), and its subsequent acceptance as an important routine investigation was largely based on his work.

Rationale /

Rationale of the Test.

Normally, arterial blood collected from a main artery of the general circulation has an oxygen capacity of 21%. However, blood in passing through the lungs does not take up its entire quota of oxygen, so that the blood usually has an oxygen content of about 20% by volume, or, in other words, it has taken up 95% of its quota by oxygen. The percentage of saturation of oxygen is calculated from the ratio of the oxygen content to the oxygen capacity, i.e.

$$O_2 \text{ Saturation} = \frac{O_2 \text{ Content}}{O_2 \text{ Capacity}} \times 100.$$

The blood in passing through the capillaries of the tissues loses approximately 25% of its oxygen, which leaves in the venous blood an oxygen content of 14% by volume or an oxygen saturation of 70%.

The readings can thus be expressed in terms either of the saturation or of the content of oxygen, both being regularly used. The saturation is given as a percentage. The normal figures for the content are recorded as 18-23 c.cs per 100 c.cs or 18-23 volumes per cent for arterial blood, and 14 c.cs per 100 c.cs or 14 volumes per cent for venous blood.

Technique of Collection of Specimen.

The correct technique must be carefully adhered to, as a faulty method will give a useless reading. The important point is that the collection of blood must be made without any possible exposure of it to the atmosphere. Various methods have been noted but the following has proved simple and accurate.

A syringe and a long needle are sterilised, washed free of any antiseptics, and then immersed and rinsed in sterile liquid paraffin. The test tube, which is to receive the blood, contains enough calcium oxalate to prevent subsequent clotting, and is then filled with about 2-4 c.cs of liquid paraffin. Blood is then withdrawn from a suitable vein into the syringe, and is then transferred to the test tube. This step is carried out by immersing the point of the needle below the liquid paraffin and then injecting the blood, so that the latter forms a layer over it, impervious to the air. Care must be taken that no bubbles of air are introduced with the blood, as a false high reading would thus be produced. A glass rod, smeared with liquid paraffin, is then used to mix the blood with the calcium oxalate to avoid clotting, which would ruin the test.

Laboratory Estimation.

A skilled chemical analysis is entailed and

is not described here. It is the gasometric method of Van Slyke and a full account of it is given by Peters and Van Slyke (183).

Site of Collection of Specimen.

It is always desirable, in order to obtain a satisfactory control, to collect blood from a vein in a normal part, usually in the elbow region. Only thus can slight differences in readings be appreciated.

A prominent, superficial vein, proximal to the fistulae, is often chosen, as recommended by Brown (121), but in other cases, where the fistulae are in an inaccessible site, any prominent vein is selected. Horton (92) suggested in 1932 that the blood be withdrawn from deep veins, such as the femoral, conclusive results being obtained.

An important modification was introduced in 1936 by Veal and McCord (57). The technique is that the limb is elevated until blood is drained out of the veins, after which tourniquets are applied, dividing the limb into as many segments as desired. The patient then stands or the upper limb is allowed to hang by the side, so that all veins and varicosities become filled with blood. Samples of blood are then withdrawn from the different segments.

Interpretation of Results.

In cases of arterio-venous fistulae, blood withdrawn from a vein in the vicinity may give any reading from slightly above that of pure venous blood to that of almost pure arterial blood. The degree of admixture of venous blood with arterial blood indicates roughly the size of the abnormal communications.

The site of collection of specimens may be of great significance. Using blood from any prominent superficial vein, a high oxygen reading indicates one or more arterio-venous communications, but a normal reading calls for more investigation. In some cases a high reading may be obtained only from a deep vein, with normal results from all superficial veins. In other cases, the arterio-venous communications may not be sufficiently extensive to change the character of the blood throughout a limb and the diagnosis may be missed because the specimen is taken from a site too remote to be affected. By division of the limb into segments with tourniquets, different readings may be obtained, a high one in the vicinity of the fistulae and a normal one elsewhere. In this way, it may be possible to localise the site of the fistulae accurately.

The full investigation of the oxygen content

of /

of the venous blood is of such importance that it influences the diagnosis considerably. On studying accounts of cases reported before the use of the oxygen test, it seems that the diagnosis may frequently require to be reviewed and it is difficult to judge accurately the relative frequency of the various types of vascular anomaly. In particular, many cases of phlebectasis must be considered as probable examples of arterio-venous fistulae. Horton (92), for example, demonstrated that cases otherwise typical of pure phlebectasis showed a high oxygen content of the venous blood of the affected part, and on the other hand, Lee and Freeman (89) reported a similar case where blood from the femoral vein had a normal oxygen content, thus definitely excluding arterio-venous fistulae.

Oxygen estimations were made in nine of my cases. The importance of the modification of Veal and McCord was emphasised in Case Four, as a sample from the upper part of the thigh gave a high reading and one from the knee a normal result. The test was unavoidably restricted in Case Seven, where a positive result would have been anticipated. In Case One, the slight difference in readings in the two lower limbs suggested a small degree of arterio-venous communication on the one side. High oxygen readings were definite proof of arterio-venous fistulae in Cases Three, Six, Eight, Nine and Eleven, in the absence of other positive signs.

In addition to occurring in congenital vascular anomalies and haemangiomata, an abnormally high oxygen content of the venous blood is found in traumatic arterio-venous fistulae and in certain derangements of the normal arterio-venous anastomoses.

SKIN TEMPERATURE TESTS.

Increased temperature of the affected part is a very common feature of all varieties of congenital vascular abnormalities. It is most noticeable in the limbs, where part or whole of a limb may show a higher temperature than the opposite limb at a corresponding level. It may be noted in the scalp, face and neck, but is seldom so striking, as the lesions there are not so strictly unilateral. As in the traumatic arterio-venous fistulae, the temperature may be abnormally high in the region of congenital arterio-venous fistulae, while that at the distal extremity of a limb may be low when signs of impaired circulation are developing.

It is to be noted that the high temperature is not itself a diagnostic sign of arterio-venous fistulae /

fistulae and may be produced by venous stasis alone as found in gross varicosities. There is, however, probably an important relationship between the high temperature and the increased growth of the affected part.

Simple palpation by the examiner's hand will often reveal that the affected part is definitely hotter. In the most marked cases, the excess of heat given off may be appreciated without any actual handling.

More accurate methods, however, are desirable. Finlayson (7) in 1884 was probably one of the first to make an accurate examination of the skin temperatures in such cases. Using mercury thermometers, he tested the temperatures at different levels on the limbs and face and showed a definite increase in the cheek, hand and leg on the right side. Few subsequent observers carried out such careful investigations until fairly recent years, when more convenient methods became available.

The modern instrument used for accurate skin temperature tests is that described by Grant (192) and is a portable, copper-constantan, thermo-electric couple. There is a sensitive but robust pointer galvanometer and the temperature is read directly from the galvanometer scale. Several leads are available to be attached at different levels of the affected part and of the corresponding opposite side, the limbs being the commonest parts to be examined.

In carrying out the usual test, the limbs are exposed at room temperature until their temperatures are stabilised, and thereafter readings are taken on the two sides at corresponding levels simultaneously. A difference of several degrees is demonstrable in many cases and was well exemplified in Cases Three, Four, Eight and Eleven.

An extension of the test is the determination of the vasomotor reaction of the part. After stabilisation of the temperature of the limbs at a constant room temperature, if the lower limbs are to be examined, the hands are immersed in water at 43-46°C, or, in the case of the upper limbs, the feet are immersed. In the absence of any coincident spastic or obliterative vascular disease, there is a sharp rise in the temperature of the two limbs, which tends to be more sudden and higher in the affected side than on the normal or control side. Such a finding was present in Cases One and Three.

A /

A further test of a different nature is the estimation of the amount of heat eliminated by the affected part, measured in Calories per minute. Horton (92) noted readings varying from 17 on the normal limb to as much as 600 in the abnormal limb in a severe case. This test was not carried out in my cases.

OTHER TESTS.

Circulation Time.

Estimations have been made in cases of traumatic arterio-venous fistulae but seldom in congenital cases and not in any of my own. Several methods are available such as the sodium cyanide method and the decholin method. Using the former, Reid and McGuire (77) demonstrated, in traumatic cases, an acceleration of the circulation time when the drug was injected into a vein between the fistula and the heart, a retardation on injection into a vein distal to the fistula, and no change on injection into veins in a normal part of the body.

Blood Volume.

Changes in the blood volume have been described in traumatic arterio-venous fistulae, but there is no unanimity on the subject. Holman (61) demonstrated a definite increase in blood volume, but Reid and McGuire (77) failed to confirm this, except in the presence of advanced cardiac failure. The test has only rarely been studied in congenital cases, e.g. by Pemberton and Saint (35), and investigations carried out in three of my cases were not conclusive.

Venous Pressure.

Venous pressure, likewise, has often been investigated in traumatic cases but seldom in congenital abnormalities. When the arterial pressure is transmitted through a fistula into a vein, the local venous pressure does not tend to remain at a high level, on account of the resulting dilatation of the vein and the increase in capacity of the venous bed. The pressure is highest in a vein near the fistula, is less in a vein beyond, and varies according to the size of the fistula. An increase in the general venous pressure occurs in the late stages, when severe cardiac failure has developed.

It is to be noted that the local venous pressure is greatly influenced by posture, so that the value of the estimation is doubtful. The direct method /

method of measurement consists in placing a manometer in communication with a vein by means of rubber tubing and a needle, the normal figures being 5-15 cms. of water and abnormal readings reaching to 30 cms. of water in congestive heart failure. Kennedy and Burwell (133) recorded a pressure of 45.5 cms. of water in a superficial vein in immediate proximity to the fistulae in a case of probable traumatic origin.

S E C T I O N S I X.

EMBRYOLOGICAL CONSIDERATIONS.

NORMAL GENESIS of BLOOD VESSELS.

Early Development.

The earliest changes in the development of blood vessels are not known with complete accuracy, and, though there is general agreement on many points, separate theories have been advanced, such as the angioblastic theory and the local origin theory. References to the subject are to be obtained in the writings of Keith (196), Sabin (161), and Seeger (78) and in Cunningham's Anatomy (197).

The first appearance of the development of blood vessels is to be found between the mesodermal and entodermal layers of the wall of the yolk sac and thus entirely outside the embryo. The vasoformative cells are generally believed to be derived from the mesenchymal stratum of the mesoderm, though it has been suggested that the entoderm is the source. The earliest appearance in the embryonic area, however, follows later and is probably in the splanchnic mesoderm of the pericardial region. At the seat of origin on the wall of the yolk sac, the cell bodies of the vasoformative cells or angioblasts are continuous and form a syncytium, but later they become vacuolated, so that fluid collects within them. By differentiation of certain cells, a blood island is formed, composed of a blood space, cells within it and enclosing endothelium. These blood islands, scattered over the yolk sac, become confluent by the union and canalisation of intervening endothelial cells, and thus a vascular network is produced on the yolk sac. It is on the subsequent changes that difference of opinion is chiefly expressed.

The angioblastic theory. His believed that certain cells on the yolk sac, already mentioned, undergo early differentiation to form specialised tissue, from which the endothelium of the yolk sac vessels and the blood cells are exclusively derived. The cell, termed the angioblast of His, produces this precociously developed vascular tissue, which is regarded as forming a local unit vascular anlage. The angioblast then grows into the embryonic axis from the yolk sac in a continuous and uninterrupted manner, thereby supplying to the embryo all the material which subsequently gives rise /

rise to the endothelium of the entire intra-embryonic vascular system.

The local origin theory. According to this, mesenchyme may become a vascular tissue in almost every region of the body. The cells which bound on the intra-embryonic blood vessel are not in direct lineage with those which line the early vessels on the yolk sac. They have not come into being as an ingrowth from early yolk sac vessels nor from angioblasts, and they have not necessarily come from pre-existing endothelial cells. Endothelium may be added to in several ways:- (a) by proliferation of endothelial cells already formed; (b) by addition of single mesenchyme cells; (c) by addition of solid cell aggregates; (d) by addition of already formed endothelial cavities, the lining cells of which have differentiated locally, in and from mesenchyme; (e) by active migration and alignment of single mesenchyme cells to form vascular cavities.

That doubt on these processes of development can exist is shown by the changes of view of such an eminent authority as Florence Sabin. In 1918 (161) she expressed the opinion that blood vessels first arise not only in the membranes, but also in the embryo, by differentiation of cells into angioblasts by the process which His described, and not from dilatation of spaces in the mesenchyme and the flattening out of cells to form their border. Later it was stated by Seeger (78) that Sabin favoured a theory that there is a limited period for differentiation and growth of angioblasts out of undifferentiated mesenchyme, and that after this period all new blood vessels arise from the growth or proliferation of older angioblasts. Still another theory advanced by her is that angioblasts continue to differentiate out of mesenchyme indefinitely.

McClure, also quoted by Seeger, stated that the angioblast theory as proclaimed by His no longer holds and he voiced his belief that the theory of local genesis of endothelium is an established fact, a view not challenged since.

Subsequent Development.

Seeger (78) quoted Jordan in stating that the final anastomosing sprouts of endothelium represent definitive capillaries and that uncertainty concerns the point in time when vasculogenesis passes from the process of sprouting and fusion of anlages to one when extension occurs solely by terminal growth. Both arteries and veins have a like origin in the capillary plexus.

Rienhoff /

Rienhoff (22) described how the anlage of the blood vascular system differentiates out, for each separate region of the embryo, as a primary capillary network which is very rich in anastomoses and through which the flow of blood is very slow. A definitive vascular tree is then evolved from this network by the gradual coalescence of the more fortuitously placed capillaries, and an atrophy and disappearance of those less favourably situated. In the course of development, the paths taken by the blood stream are remarkably definite for each region. Cardiac impulses, as well as other hydrodynamical factors, play an important part in the determination of the vascular bed, but the greatest factor is the inherent tendency of certain embryonic tissues to form certain definite structures.

After the angioblastic stage, three stages are to be distinguished in the formation of an individual arterial tube, according to the views of Woollard (160) and of Sabin, as quoted by Mason (172):- (1) the stage of the capillary net; (2) the retiform stage, characterised by enlarged tubes, showing coalescence and a tendency to fuse; (3) the formation of a definite stem.

FORMATION of ABNORMAL ARTERIO-VENOUS FISTULAE.

Important experimental embryological work has been performed in an attempt to trace the earliest stages of these abnormalities. Sabin, quoted by Halsted (15), carried out experiments on the chick and noted that the anterior half of the yolk sac is venous while the posterior part is arterial. Thus the omphalo-mesenteric veins and arteries are separated as far as possible by a wide capillary bed. Originally the arteries lie throughout their course in a capillary network, and, in the capillaries along the caudal border of the artery, the blood flows away from the heart, while, in those along the cephalic border, it returns directly to the heart. As the chick develops, these two sets of capillaries along the main stem of the artery lose their connections with it and join each other, thus making a plexus which accompanies the artery and in which develops the vein. It is obvious that the retention of any of the original connections of these capillaries with the artery will form the basis of a direct anastomosis between artery and vein. Another experiment of Sabin's was quoted by Rienhoff, in which, by the injection of a toxin, she produced an arterio-venous fistula in the area vasculosa of a chick, between the omphalo-mesenteric artery and vein.

Rienhoff (22) also carried out experiments on the area vasculosa of chick embryos, studied microscopically by means of a window in the egg shell over /

over the blastoderm. A large number of capillary communications, which ultimately atrophy, were noted to persist between the arterial and the venous trunks for several hours after the larger vessels were fairly well formed. As soon as the environment was caused to become detrimental, an unusual and bizarre formation took place. In one experiment, one of these capillary communications became much larger and took over the greater part of the blood flowing through the artery. The artery then became enlarged proximal to the fistula and smaller distal to it, while the vein became enlarged on both sides.

Woollard (160), studying the fore limb of pig embryos, was able to show, when the subclavian artery and vein were beginning to be differentiated, that there were multitudinous free communications between the two vessels. Should any of these persist, perhaps due to some detrimental influence, then permanent arterio-venous communications will be produced, and it thus seems certain that the multiple nature of congenital arterio-venous fistulae can be explained. Reid, in fact, commented that it was surprising that direct congenital communications do not persist between large arteries and veins more frequently than they do, considering the widespread nature at one stage of development. Patent foramen ovale, patent inter-ventricular septum and patent ductus arteriosus are other well recognised types of congenital communications between the arterial and the venous blood streams, but they are obviously due to disorders of a different nature and are not discussed here.

Chandler (62) indicated that faulty development of the vascular tree points to some factor active in the fourth week of embryonic life. Should this factor continue over a long period or develop later, a distortion of the lymphatic system may be a complication.

As a result of the above survey of embryological details, there appears to be a solid background for the view that arterio-venous fistula and haemangioma can be traced to an error at one of the stages in the development of the vascular system. The significance will be discussed in the section on pathology and etiology.

S E C T I O N S E V E N.

DISCUSSION on PATHOLOGY and ETIOLOGY.

ORIGIN and NATURE of SIMPLE ANGIOMA, PHLEBECTASIS, CIRSOID ANEURYSM and ARTERIO-VENOUS ANEURYSM.

Terminology.

The scope of the thesis is not intended to cover an investigation into the subject of blood vessel tumours. In the study of my personal series of congenital vascular anomalies, certain conditions, usually designated as haemangiomata, were encountered, and it thus became essential to review the opinions on haemangiomata in general and their relationship to congenital vascular anomalies in particular. All cases not truly congenital in origin have been omitted, for example, traumatic or spontaneous cirsoid or arterio-venous aneurysms, or the rare Kaposi's haemorrhagic sarcoma. Enough has been mentioned in previous sections about the confused nomenclature of the vascular lesions in question. One difficulty appears to have been that lesions have been too rigidly classified according to the tissues and the site in which they were most prominent, to the clinical appearances only, to the pathological appearances only, to the effects of treatment only, or to their single or multiple development only; thus these have been few comprehensive accounts of the widespread and extraordinarily varied manifestations. The term naevus is applied both to a haemangioma and to the entirely different condition of melanoma, a most unfortunate type of nomenclature. It should either be reserved solely for the latter condition or else avoided completely.

It is intended now to state the views of several selected authorities on the pathology and etiology of vascular tumours and anomalies in general, without particular reference to the occurrence in any special tissue or site; many inconsistencies are to be found, however. Thereafter, an attempt will be made to correlate such views, and opinions based on personal observations will be introduced.

Review of Previous Opinions.

Ewing (168) mentioned many different varieties of haemangioma. The haemangioma simplex, although classified as a tumour, has its origin referred to a developmental anomaly in the structure of several vascular segments, which does not fit into the circulatory /

circulatory system and which retains embryonal characters; one subtype, the plexiform angioma, consists of a new growth of dilated capillaries. The cavernous angioma in its growth shows mechanical dilatation of the veins, and also proliferation of connective tissue, said to be indicative of tumour growth. A racemose arterial angioma or cirsoid aneurysm was believed to belong to a class of partial neoplasms.

Fraser (175) defined a haemangioma as a tumour in which there is actual new formation of vessels or proliferation of the vessel walls, and he stated that it grows from rests of embryonic mesenchymal tissue. Three types were described, the capillary, the cavernous and the compact. The capillary type consists of a collection of embryonic blood vessels, the cells of which show division and mitotic figures; smaller arteries, veins and capillaries circulate between the tumour elements. Natural arrest or further spread may take place. The cavernous type develops after the embryonic capillary tissue obtains a connection with the circulation. The compact variety may develop if endothelial cells of the capillary type take on active proliferation, either endovascular or perivascular. Shaw (176) supported these views.

Watson and McCarthy (164) believed that simple angiomas are congenital in nature, have their origin in embryonic sequestrations of mesodermal tissues and grow by projecting buds of endothelial tissue. Such a tumour inherits from its embryonic parent a certain power of irregular and unrestrained rapid growth. The racemose or cirsoid type was believed to establish a communication with surrounding normal blood vessels. The authors admitted the difficulty of a rigid classification and mentioned eight types of haemangioma:- capillary, cavernous, angioblastic, racemose, diffuse systemic, metastasising, port-wine stain and hereditary haemorrhagic telangiectasia. One of their illustrations, depicting a systemic haemangioma, gave the appearances of a typical vascular anomaly.

Kidner (59), in discussing cavernous angioma, spoke of it as a congenital tumour, arising from abnormally developing embryonal tissue and capable of being infiltrative and destructive. Stewart and Bettin (24) classified haemangiomata as real tumours, congenital in origin, and of three types, capillary, cavernous and plexiform. Davis and Kitlowski (13b) reported cases of angioma of muscle and believed them to be tumours arising in a congenital anomaly, trauma being a factor in their growth.

Bland /

Bland Sutton (127) stated that an angioma is a tumour composed of an abnormal formation of blood vessels. Nemenov (83), reporting on haemangioma of bone, stated that angiomas in any tissue are true tumours. Fitzwilliams (179) considered that there were two classes of naevus, the common form composed of endothelial spaces, and the less common extensive naevoid consisting of dilated vessels, chiefly capillaries. These were tumours, and to be excluded from them were cirsoids, abnormal connections between arteries and veins, and varicosities.

Rankin and Chumley, quoted by Laird (103), while admitting the difficulty of classification, enumerated three groups:- angioma simplex or capillary angioma; angioma cavernosum; angioma simplex hypertrophicum or angioendothelioma. Lesions resembling true neoplasms fall into the third group and arterio-venous fistulae are variations of the first and second group or are a separate entity.

MacCallum (163a) admitted the difficulty of deciding whether certain border line cases are tumours or not, such as plexiform or cirsoid angiomata of the scalp, made up of tangled masses of pulsating arteries, and others such as bluish vascular flecks in the skin of old people. True haemangiomata were divided into the simple or telangiectacic form and the cavernous form. They were believed to be tumours growing independently from a rudiment destined to form blood vessels, and one should abandon ideas as to their being due to mere dilatation of capillaries. A cirsoid or racemose aneurysm is perhaps a sort of tumour, in which tangled wide blood channels are newly formed as an abnormal and independent growth, still fed with blood from the general circulation, or possibly as a result of congenital arterio-venous communications.

The work of Ribbert has been reported by several authorities and given much publicity. By means of interstitial injections of angiomata, he found that the vessels had few or no lateral anastomoses, while the injected medium passed freely into an afferent artery and efferent veins. He described the growth of an angioma from its own angioblastic embryonic tissue and opposed the view that it grows from the widening and assimilation of pre-existing adjacent blood vessels. MacCallum (163a), Shaw (176) and Watson and McCarthy (164) maintained that these findings indicated that an angioma was a tumour, whereas Reid (73) believed that the work rather supported his own conception of an angioma as being an anomaly and not a tumour.

Reid (73) and Laskey (47), among others,

have/

have quoted various independent views which have been expressed on the etiology and pathology of angioma and cirsoid aneurysm. Aschoff was inclined to treat angiomata as neoplasms or partial neoplasms arising from a displaced segment of the vascular bed, which comes to possess a limited power of an aberrant growth; a cirsoid aneurysm was reckoned to be an arterial angioma. Rokitansky and Borst regarded an angioma as a simple hypertrophy of vascular segments without neoplastic overgrowth, and Thoma considered mechanical factors important in the growth of angiomas. A cirsoid aneurysm was regarded as an arterial tumour by Matas, Delafield and Prudden, and Gross, and as due to inflammation by Billroth. Ashurst noted that not only arteries but also veins and capillaries were dilated in a cirsoid aneurysm, and Halsted cited the similarity between a cirsoid aneurysm and arterio-venous abnormalities. Stanley, Wright, Wernher, Thorndike, Cohen and Warren noted free communications between arteries and veins in cirsoid aneurysms, and believed the cause to be arterio-venous anastomoses.

McFarland (23) designated an angioma as a tumour composed of newly formed vessels. Though agreeing with Adami, he gave a different classification:- A. Angiomatoids, including varicose aneurysms, cirsoid aneurysms, vascular hypertrophies and telangiectases; B. Angiomata, including angioma simplex, haemangio-endothelioma, and cavernous haemangioma, capable of pulsation when large.

Duncan (10) included many varied appearances under the title of angioma, but he did not give any rigid pathological details about the presence or absence of tumour growth. Parkes Weber (116) spoke of a tumour-like haemangiomatous growth, with dilatation of arterial and venous trunks, and associated with a congenital or developmental hypertrophy of the affected part. Phlebectasis, phlebarteriectasis, cirsoid aneurysm and plexiform haemangioma were believed to be of the same probable nature.

Albrecht, quoted by several writers, such as Reid (73) and Adami (167), realised the difficulty of the classifications of haemangioma, and suggested the term "Hamartoma" to cover vascular anomalies, meaning a condition due to developmental defects. Bucy (135) in writing on angioma of bone, concluded that nothing threw light on the etiology of these bony lesions, and he was unable to decide whether they are neoplasms or vascular malformations.

Harvey, Dawson and Innes (147) included all angiomata /

angiomata under the term endothelioma, which was admitted to be a debatable tumour. They defined an endothelioma either as a congenital mesodermic malformation having a tendency to disproportionate growth or as a primary neoplasm. There is a characteristic endothelial cell proliferation, which, according to the site, may be mesenchymal and vasoformative, giving rise to angiomata, or mesothelial and membrano-formative. The authors maintained that there is little point in stressing too much the difference between a vascular congenital malformation and a true tumour, and they considered it acceptable to take the term angioma as including any pathological vascular proliferation which is not regenerative, inflammatory or a mechanical disturbance of normal circulatory arrangements.

Oughterson and Tennant (171) gave the following classification:- (1) Angioma (a) Vascular malformations, including arterio-venous fistulae, telangiectases, venous or arterial angioma; (b) Angioblastoma. (2) Angio-myo-neuroma.

Muir (166) believed that angiomata are probably always due to abnormalities in the process of development rather than to true tumours. Mason (172) was of the opinion that the various forms of angiomata can be related to errors at different stages of development of the vascular system, and he mentioned four classes of angioma:- angioblastic (very rare), telangiectatic, cavernous, and the vessel type.

Lee, W.E. and Freeman (89) did not give any specific views on the nature of an angioma, but they stated that free communications between an angioma and the arterial side of the circulation lead to a cirsoid aneurysm, and between an angioma and incompetent veins in the lower limb to a venous angioma. Berry (12) believed that a cirsoid aneurysm really consists of dilated tortuous veins rather than arteries, and he did not mention any possibility of tumour growth. Colley (88) considered all cirsoid aneurysms to be due to a developmental defect, even although arising on the site of a cavernous angioma. Beluffi (63) concluded that a cirsoid aneurysm is not a true tumour and that it is a complex of purely mechanical vascular changes, secondary to the formation of multiple peripheral arterio-venous anastomoses.

Adami (167) stated that the majority of so-called angiomas, or tumours having vessels as their main constituent, are spurious blastomes, with no power of independent growth, and that mere dilatation and filling of vessel spaces with fluid is not a growth. A cell rest, or inclusion within a tissue, is not a blastome so long as it lies latent and is not growing /

growing, and similarly a mass of tissue which is aberrant in structure due to a developmental defect is not a blastome. In the majority of cases, the evident increase in the length of vessels or thickening of the walls is not in excess of physiological requirements and there is no evidence of proliferative capacity. The conception of the word angioma is important and it would make for precision to remove most of the conditions now included under the heading of angioma and to place them under the class of, say, telengiectases. If one means simply a swelling composed of blood vessels, then all cases remain as angiomas; if one restricts the term to mean a tumour, due to independent growth of blood vessels, then most cases must be cast out.

The following classification was proposed:-

Group A. Blood Vessel Tumours (Haemangiomas) which are not blastomes:-
(1) Obstructive Telangiectases, including varicosities; (2) Aneurysms; (3) Congenital Telangiectases, (a) Telangiectatic Naevus, (b) Cavernoma, showing no sign of independent growth.

Group B. True Typical Blastomatous Haemangioma - Angioma Simplex - in which there is a progressive new development of capillaries; usually simple, very rarely malignant.

Rienhoff (22) indicated that all congenital blood vessel tumours are due to the persistence of embryonic vascular channels and are in no sense of the nature of neoplasms. It was proposed that they arise from either an arterial plexus or a venous plexus of the primary vascular anlage, or from a combination of the two. It was also emphasised that the close association of haemangioma and congenital arterio-venous fistula is very suggestive of the same etiology.

Reid (73) gave very full reports on angiomata, cirsoid and arterio-venous aneurysms. Dealing with cirsoid aneurysm, he noted how it and arterio-venous aneurysm can be due both to congenital and acquired causes, and he expressed the opinion that there is no difference between them, except that a cirsoid aneurysm results from small arterio-venous communications in the more peripheral and smaller vessels. He indicated also that a cirsoid aneurysm is in no sense a neoplasm and that its main mass is composed of dilated veins. On the controversial subject of angioma, he noted that vascular endothelium may give rise to tumours with the property of independent growth or even metastases, such as haemangioendothelioma, pigmented naevus, and haemangioma simplex, but that the great majority of angiomas are composed simply of swollen /

swollen blood vessels and do not exhibit the qualities of true neoplasms. Although his researches did not furnish definite proof of the etiology of simple angiomas, Reid believed that they are due to dilatations of small arteries and veins caused by abnormal communications between arterioles and venules. In support of his views, angiomas possess many points of similarity to arterio-venous aneurysms and cirsoid aneurysms which differ only in their pulsatile nature and rapid enlargement. Angiomas may grow, become more susceptible to strains such as crying or pregnancy, begin to pulsate, develop free anastomoses between arteries and veins, and soon exhibit all the clinical features of a true cirsoid aneurysm. Their fate is probably determined by the freeness of their anastomoses and the strains to which subjected. Small naevi may disappear spontaneously and large angiomata may disappear either spontaneously, or as the result of inflammation, thrombosis or slight surgical intervention. Reid concluded that these features are most unlike those of a neoplasm and that, in the light of the work of Sabin and Woollard, congenital anomalies are easily understood.

Homans (86) noted how all congenital arterio-venous communications are apt to be called angiomata or haemangiomata, with the implication that they are actually tumours. The arterio-venous malformation, however, rarely grows in the sense that the parts multiply, and it enlarges as the result of dilatation of blood vessels or blood spaces. The simplest degree is a swelling composed of undifferentiated spaces, neither arterial nor venous; such is the naevus, which may be capillary or cavernous, and which may be covered by normal skin, or by a port wine discolouration of the skin, or by a mixture of the two. It makes a great difference whether the malformation occurs in the vascular bed of the skin and subcutaneous tissues or in the great vessels. Both capillary and cavernous haemangiomata are supplied with arterial blood, which has so little force that they never pulsate, the tissue merely resembling a very vascular sponge with smaller or larger meshes. Another type has more direct connections by a series of tiny vessels, but there need be no actual pulsation in the veins, nor any bruit nor thrill; the blood in prominent veins shows a slightly raised oxygen content. Occasionally, a relatively quiet form is injured or undergoes some other change, so that the afferent artery is liable to pour a large stream directly into the lesion; a cirsoid aneurysm may thus be formed, especially in the scalp. Arterio-venous aneurysm or fistula is especially common at the root of the neck or of a limb, because at these sites great arteries and veins lie

in /

in close contact and are held together in a fibrous sheath. If they are malformed, i.e. not fully differentiated, there may be multiple fistulae, a series of small channels making connections over a considerable distance. The fistula is usually defined as a direct opening or simple narrow passage, whereas the aneurysm is held to be a sacculation interposed between artery and vein.

Craig and Horton (99) mentioned the confusion relating to names such as cirsoid aneurysm, arterio-venous aneurysm, pulsating venous aneurysm, arterio-venous varix, aneurysma serpentina, angioma plexiforme, angioma arteriale, angioma arteriale serpentinum, and angioma arteriale racemosum. They emphasised that, in all these, the fundamental condition is arterio-venous fistulae. Ward, C.E. and Horton (98) indicated that any variation from the normal capillary communications, in the direction of dilatation, constitutes an abnormal arterio-venous communication.

De Takats (51) considered that a vascular tumour or angioma is not a true new growth but is due to faulty development and that it is only an angiectasis, that is, a dilatation and lengthening of arteries or veins or both. Many variations are encountered, such as angioma simplex, cavernous and racemose angioma, diffuse phlebectasis and congenital arterio-venous fistula but all can be explained by the stage in vascular development in which the aberration from normal occurred. Following the descriptions by Sabin and Woollard, as mentioned in the previous section, de Takats recognised the capillary net stage, the retiform stage and the definite stem stage and traced the abnormalities accordingly. Thus, the capillary angioma is a localised remnant of the primitive capillary net, remaining as a harmless birthmark. Often precipitated by trauma, a sudden connection with the general circulation may start feeding it with blood, and a progressive cavernous dilatation then develops which may grow destructively owing to a continuously increased pressure. Diffuse phlebectasis and congenital arterio-venous communications take origin in the retiform stage. A number of parallel vascular tubes, insufficiently fused, are connected by communications, which in some instances are only a few and tiny, and in others are innumerable, in which case progressive gangrene usually results. Finally, it is also conceivable that the vascular development may reach the third stage of definite stem formation. One of the primitive vessels may persist and present an anomalous primitive trunk in an abnormal site and with a histological structure which does not correspond to that of either an artery nor of a vein.

Though/

Though intracranial vascular lesions are not included in the scope of the discussion, it is of interest to compare their terminology with those already mentioned, differences of opinion again being admitted. Cushing and Bailey (170) classified them as follows:- (1) Vascular malformations - (a) telangiectases, (b) venous angioma, (c) arterial angioma; (2) Haemangioblastomata - less common, situated in the cerebellum, cystic or solid. Northfield (126) under the heading of angiomatous malformations of the brain, included:- (1) Cavernous angioma; (2) Telangiectases; (3) Racemose angioma - (a) venous angioma, (b) Sturge-Weber syndrome, (c) arterial angioma, (d) arterio-venous angioma. These views therefore tend to show that vascular malformations and not tumours are the cause of most so-called haemangiomata involving the brain. Another intracranial vascular malformation is the rare congenital carotid-cavernous sinus fistula, a case being described by Reid (72), in which pulsating exophthalmos is the outstanding feature.

Correlation of the Various Views on Etiology.

Many differences of opinion, sometimes quite contradictory, are evidenced, but yet it seems certain that these divergencies must be less serious than indicated and that some factor, common to all theories, is always present. Search for such a common factor reveals that the congenital nature of angiomata and vascular abnormalities alone commands unanimity, although both an embryonic sequestration of mesodermal tissue and a malformation of the developing vessels are suggested. Accounts have already been given of the normal development of the blood vascular system and of the formation of abnormal arterio-venous fistulae, and it has been shown how all the congenital anomalies can be traced to an error in development. It seems that on an embryological basis, it may be possible to explain the occurrence of both tumours and anomalies and to reconcile opposing views.

On examining the early development, there is a stage before any actual vessels have formed, at which masses of angioblastic cells are present. A collection of these cells may fail to mature and may then remain in the tissues as an embryonic rest, dormant but capable of active growth at any time thereafter. Alternatively, these cells may be submitted to some deleterious influence so that their growth thereafter is abnormal. By such means a true tumour, derived from vascular endothelium, may be produced, and in this group may be included the compact angioma, the angioma simplex, the capillary angioma with sprouting buds of endothelium, and the rare malignant angioma.

If the development proceed to the stage of capillary net, and an interruption then take place, a portion of this net, of varying size, may remain sequestrated and fail to pass on to the next stage. Thus can be accounted for the formation of a capillary angioma, without any endothelial proliferation, which it is probably correct to classify as an anomaly rather than a tumour.

The development having reached the next or retiform stage, the original angioblastic cells have become mature and unlikely to be capable of independent unrestrained growth. Any interruption now will tend to produce an abnormal development with failure of separation of the arterial and venous trunks from the original capillary plexus. Excessive communications may remain between veins and capillaries, the condition of phlebectasis resulting, or they may persist between main arterial and venous trunks causing arterio-venous fistulae or between smaller trunks producing a cirsoid aneurysm.

If the earlier stages are passed through without mishap, it is possible for an abnormality to develop at the stem stage, in which case there results a vascular trunk in an abnormal site and of an indeterminate structure.

Typical Pathological Variations.

From a study of the various theories on pathology and etiology, it is evident that there is no completely satisfactory classification of the various congenital vascular tumours and anomalies. As with the clinical features, however, it is perhaps desirable to review, on a broad basis, the most important pathological features of certain angiomata, phlebectasis, cirsoid aneurysm and arterio-venous aneurysm.

The capillary haemangioma is composed of a meshwork of small spaces lined by vascular endothelium and containing a few blood corpuscles; sometimes there may be sprouting or proliferation of endothelial cells. Spontaneous regression, particularly in the first year of life, is well known, a fact generally believed to be more in keeping with an abnormal development than with a tumour growth. On the other hand, the lesion at any time may enlarge and assume some of the characteristics of a cavernous haemangioma.

The compact haemangioma, more rare, consists of solid masses of endothelial cells, without any trace of a lumen.

The /

The cavernous haemangioma is more variable in its structure and is by no means a well defined entity. It is composed of large irregular blood spaces or veins of different size, opening abundantly into each other. These are usually lined by normal endothelium, but occasionally there is proliferation of the endothelial cells. In addition to appearing as a primary lesion, it may arise as an extension of a capillary haemangioma, especially after injury or strain. The blood in a cavernous haemangioma is connected with that of the general circulation, as can be seen after filling of the lesion after aspiration, and it may vary from venous to almost purely arterial. Spontaneous regression may take place as the result of thrombosis in the vessels, or the lesion may enlarge, begin to pulsate and assume the characteristics of a cirsoid or arterio-venous aneurysm, in which case the term cavernous haemangioma should no longer be used.

Phlebectasis or venous haemangioma is a condition featuring a gross overdevelopment of thin-walled, distended tortuous veins, which tend to show a normal structure without endothelial proliferation. The cause is generally assumed to be an error in the development of the venous system whereby numerous abnormal connections persist between main veins and extensive plexuses of smaller veins. In its true state, it is probably not as common as was once believed, as it has been shown that small unsuspected arterio-venous fistulae may co-exist. There are marked resemblances to the common type of varicose veins of the lower limb, such as incompetence of the venous valves and the mechanical effects of venous stasis.

The cirsoid aneurysm was formerly believed to be an arterial tumour or an abnormality of the arteries, but the most probable and recent view is that it is due to arterio-venous fistulae and that its main mass is composed of veins. It is generally found in relation to one small artery and vein in the scalp, neck, hand, or foot, the superficial temporal being the most common. One or more fistulae exist between the artery and vein, and thus arterial blood at high pressure enters the veins, producing their progressive dilatation, until finally all the neighbouring veins become involved. Subsequently, as mentioned also under arterio-venous fistulae, the artery proximal to the fistulae becomes tortuous, dilated and thin-walled, whereas the veins tend to become hypertrophied. Thereafter it is considered possible, especially after an injury or a strain, that the thin-walled artery may rupture into the mass of veins around it, so that new arterio-venous fistulae become established and an increase /

increase in size of the whole lesion takes place. A vicious circle is also produced, for, as the vessels dilate, so do the fistulae which are responsible for their dilatation. A type of vessel, intermediate in structure between an artery and a vein, is sometimes encountered. This may be a true aberration of the stem stage of vascular development, or it may simply be a thin-walled artery or an unduly hypertrophied vein. The vessels of the cirsoid aneurysm may be lined by normal endothelium, but at times there may be definite endothelial proliferation, chiefly in the veins and slightly in the arteries.

Another important feature of the cirsoid aneurysm is that the arterio-venous fistulae are a strong stimulus to the formation of a collateral circulation, so that adjacent arteries and veins in turn become dilated. This development becomes excessive and these arteries later obtain a connection with the vessels of the lesion and account for its further spread and still greater increase in size. Ultimately the pulsating mass of veins, forming the main mass of the cirsoid aneurysm, becomes fed not only by its original artery, but also by several others, for example, in the common site in the scalp, the opposite superficial temporal, and both supraorbitals and occipitals. This conception of the growth of a cirsoid aneurysm is almost certainly the correct one, ruling out the theory of a tumour of blood vessels which by its growth invades adjacent vessels.

Arterio-venous fistulae are due to an abnormal development so that persistent channels of communication remain between arteries and veins. It is of interest to compare their size with that of normal vessels, but it is an unfortunate fact, deplored by Seeger (78), that the knowledge of capillaries is scanty, although Krogh (162) has given a long account of the subject. According to Seeger, it is stated in Gray's Anatomy that the capillaries vary from 1/3000 to 1/2000 of an inch in diameter, and from 1/30 to 1/20 of an inch in length, and in Cunningham's Anatomy that the average diameter varies from 8μ to 12.5μ and the average length is 0.75 mm. The normal arterio-venous anastomoses, to be discussed in a separate section, were stated by Seeger to have a diameter of about 0.02 mm. and by Popoff (159) to have a diameter of less than 0.1 mm. and an average length of 0.5 to 0.8 mm. On the other hand, Rienhoff (22) reported congenital arterio-venous fistulae as reaching a length of 3 cms. In my own series of cases, the fistulous communications, although not as large as some reported, were several millimetres in diameter, and could be easily identified and handled on naked eye examination. It is certain, therefore, that the fistulae are much larger than /

than capillaries, and it is most improbable that capillaries can ever dilate to the extent of producing the signs of arterio-venous fistulae, such as pulsation in the veins, although the report of the case of Bockenheimer in 1907 gave this explanation. In general, congenital fistulae are small in size compared to traumatic.

Another distinguishing feature of congenital fistulae is their multiplicity, and only on very rare occasions has a solitary communication been confirmed. It is seldom possible to be dogmatic on their exact number, as there is a disturbing and dangerous tendency for latent unsuspected fistulae to become patent and active, perhaps after successful treatment of the original ones. The design of a fistula is variable. There may be a relatively direct communication passing between adjacent surfaces of a main artery and vein, or the fistula may be more indirect, leaving as a branch of a main artery and then merging imperceptibly with a large venous plexus.

Certain important changes are to be found in the vessels in the region of an arterio-venous fistula, much more pronounced in the traumatic case, but nevertheless demonstrable in the congenital case. The artery proximal to a fistula becomes markedly dilated and tortuous, and shows degenerative changes such as a thinning of the wall, atrophy of the muscle layer and decrease in the amount of elastic tissue. Eventually it is possible that a fusiform aneurysmal dilatation may develop or that spontaneous rupture may occur. The artery distal to the fistula is generally smaller than normal, but rarely may be dilated. In contrast, the vein in relation to the fistula becomes dilated, but shows a definite hypertrophy of its wall, with perhaps a partial development of an internal elastic lamina, which is to be explained by its increased work and adaptation to heightened pressures. These changes, called by Reid "venefecation" of the artery and "arterialisation" of the vein, are also found in a typical cirsoid aneurysm, and no doubt explain the difficulty of deciding whether the main mass of the lesion is composed of arteries or veins or an intermediate type of anomalous vessel. Calcification is occasionally noted in both artery and vein in the immediate neighbourhood of the fistula. There is seldom, if ever, any real aneurysm in relation to the artery at the exact site of the fistula, as is typical of many traumatic cases. Any such swelling is either a dilatation or sacculation of the vein and thus the terms congenital arterio-venous aneurysm, and cirsoid aneurysm also, though expressive, are not strictly accurate: it is probably better to substitute the term arterio /

arterio-venous fistulae. Another feature, which will receive further consideration, is the development of a collateral circulation. Finally, superficial veins at a distance from the fistulae tend to become dilated but thin walled, as the heightened pressure is scarcely transmitted to them, and no stimulus to hypertrophy of the wall exists.

The Significance of Endothelial Proliferation.

This subject is admittedly a debatable one, but it assumes importance in the event of the spread of vascular lesions, and also in the development of multiple and malignant vascular tumours. Any type of vascular lesion may become more active and continue to spread widely. The protagonists of a tumour theory maintain that a haemangioma, especially the cavernous type, spreads by the proliferation of endothelial cells or, in other words, by angioblastic activity, and invades neighbouring structures, such as muscle, nerve or bone, in the same way as any infiltrative tumour. Of still more importance, it may involve adjacent arteries and veins, causing arterio-venous communications to be established, which in turn complicate the issue of still further spread. The supporters of the theory of abnormal development hold that arterio-venous fistulae may remain latent for many years, but that, once they become patent and active, the previously quiescent haemangioma undergoes extensive spread. The increase in size is therefore merely due to the mechanical effects of arterial blood at a high pressure entering abnormal blood spaces or veins. Any endothelial proliferation is reckoned to be secondary to these effects and not in any way due to tumour growth. It seems highly probable that the latter view is correct in the great majority of cases, as endothelial proliferation is either absent or is explicable on mechanical grounds.

Thus it may be rightly assumed that mere endothelial proliferation itself, whether in a so called haemangioma or in an obvious anomaly, does not necessarily denote the presence of a tumour. To cite one particular instance, Meleney (20) reported the case of a congenital cirsoid aneurysm of the neck, the excised specimen on naked eye examination being composed of fairly large vessels of different types, communicating with each other through a network of smaller vessels. In addition to other typical features of a cirsoid aneurysm, on microscopic examination, well marked proliferative changes were noted in the endothelium of veins and of vessels intermediate in type between arteries and veins, but they were relatively slight in the endothelium of arteries. There was no suggestion of tumour growth and the lesion was a definite anomaly.

Turning /

Turning now to a most severe and advanced type of lesion, it is found, contrary to the above conception, that the endothelial proliferation may very rarely assume the property of a tumour-like growth. The case reported first by Pemberton, J. and Saint (35) and later by Matas (36a) was particularly striking and important pathological findings are now recalled. All the typical features of a congenital arterio-venous aneurysm of the upper limb were present and amputation was performed through the forearm on account of gangrene. Recurrence took place in the stump but could be explained by the opening up of unsuspected fistulae higher in the limb. Disarticulation at the shoulder was in turn followed by recurrence in the chest wall and axilla. The specimen removed at this second operation showed erectile cavernous tissue and large arteries and veins with numerous communications between them. Matas believed that, though much of the change could be accounted for by the penetration of the arterial stream into the venous circulation, yet a large part was neoplastic. He considered this new growth to be of the nature of a homoplastic hyperplasia in which new blood vessels are born and multiply true to type, but with the restriction, thus differing from a malignant growth, that the vascular endothelium arrives at maturity, and does not proliferate indefinitely as an atypical embryonic tissue. The specimen removed from the axilla at a subsequent operation, however, showed an alteration in structure, and now the features were an infiltration by a network of capillaries, a preponderance of endothelial cells enclosing numerous blood channels of new formation and of variable pattern, and also large cavities or cavernous spaces. This so-called metastatic growth revealed a much more neoplastic character than the parent tumour, but it was noted that the lymph nodes were free from invasion. This case, therefore, though admittedly of a rare type, illustrated a most important type of spread. Pemberton and Saint were in no doubt that originally the lesion was the anomaly of congenital arterio-venous fistulae, and yet the characteristics altered to such an extent that Matas subsequently had no hesitation in diagnosing a tumour derived from vascular endothelium and bordering on malignancy. A more wide recognition of such a possible change would account for some of the inconsistencies so often expressed on vascular lesions. Ward, C.E. and Horton (98) and Ward, G.E. and Jonas (71) also reported cases of an allied nature which will be referred to later in dealing with malignant lesions.

An explanation must therefore be sought which will account for slight and severe degrees of endothelial proliferation and the occurrence of a tumour in a previous anomaly. Chandler (62) remarked that tissue growth is accelerated when vascular anastomoses are widespread as in arterio-venous fistulae or in an extensive /

extensive naevus, a likely explanation being the increased local temperature. It is feasible that the vascular endothelium may partake in this activity as well as other tissues, but the only confirmation to be proferred is the fact, quoting MacCallum (163b), that tissue cultures in vitro exhibit an increase in growth on gentle raising of the temperature, though not above the optimum. This suggestion, therefore, may be partly true but is of much less importance than the mechanical factors.

Meleney (20) suggested that the excessive endothelial proliferation is due to the demand made by the physical forces of an abnormal circulation in vessels not adapted or poorly adapted to withstand these forces. This seems a reasonable and sound proposition, to which the following qualifications may be added. Once the high arterial pressure is brought to bear on the veins, the endothelial proliferation is not a pathological but a physiological response, similar to the hypertrophy of the veins. It may, however, be designed to permit the production of new venous channels to cope with the increased volume of blood in the veins. As a further step, a proliferation bordering on the pathological may develop imperceptibly and produce the homoplastic hyperplasia, described by Matas, in which new blood vessels are born and multiply true to type, so that the vascular endothelium arrives at maturity. At a still later stage, the original mechanical factors adopt a less important role, and the endothelium now assumes a wild unrestrained growth, with a preponderance of solid masses of cells and irregular blood channels and spaces. This tumour may be bordering on true malignancy, as in Matas' case, or frankly malignant.

One other possibility arises in connection with these changes. It is conceivable that primitive angioblastic cells may lie dormant as a sequestration in the tissues around a vascular anomaly. After an injury or as the result of blood entering the venous system, these cells may be stimulated to assume active growth, producing the same effects as above. This conception is less likely, as there is no proof that such rests exist.

There is no novelty about the possibility of a change from a physiological response to a malignant proliferation of cells, and examples are to be found in many tissues, one being the onset of a primary liver cell cancer in the course of compensatory hyperplasia in cirrhosis.

Pathological Classification of Personal Cases.

It was not possible to consign my personal cases /

cases to any precise pathological classification of the vascular lesions, largely on account of their multiple nature. Pathological material was available in four cases, but, with sufficient clinical and operative findings, a fairly accurate diagnosis was made in every case. Case Nine was an example of a glomangioma associated with arterio-venous fistulae, but this lesion is believed by many to be an anomaly and not a true tumour. In all the other cases, evidence of tumour growth was lacking. The widespread capillary haemangiomata in several of the cases did not behave as tumours and appeared to be simple malformations.

Case One. Diffuse phlebectasis, capillary haemangiomata, an anomalous vessel and possible arterio-venous fistula.

Case Two. Diffuse phlebectasis.

Case Three. Arterio-venous fistulae, capillary haemangiomata, and an anomalous vessel.

Case Four. Arterio-venous fistulae and capillary haemangiomata.

Case Five. Arterio-venous fistulae (or cirsoid aneurysm).

Case Six. Arterio-venous fistulae (or cavernous haemangioma).

Case Seven. Arterio-venous fistulae and venous or cavernous haemangiomata.

Case Eight. Arterio-venous fistulae and venous haemangiomata.

Case Nine. Arterio-venous fistulae due to glomangioma; also three small glomangiomata.

Case Ten. Diffuse phlebectasis and capillary haemangiomata.

Case Eleven. Arterio-venous fistulae and capillary haemangiomata.

Case Twelve. Arterio-venous fistula (or cirsoid aneurysm).

IMPAIRMENT of the PERIPHERAL CIRCULATION.

The clinical features of the abnormal state of the circulation in congenital vascular anomalies have already been detailed. There remain to be discussed /

discussed the important pathological and etiological factors in the impaired circulation of a limb the site of congenital arterio-venous fistulae. The effects tend to be more grave and more often necessitate amputation in congenital than in traumatic cases.

In congenital cases, in spite of the clinical features of an abnormal circulation, the blood supply to the hands and feet, especially the digits, may remain adequate for many years. Thereafter, there may be the insidious appearance of a deficient blood supply, evidenced by chronic ulceration of the digits, haemorrhage, pain and cyanosis. Temporary healing of the ulcers may take place, but ultimately frank gangrene results, limited at first usually to one or two digits and then spreading to the adjacent part of the hand or foot. After amputation, a serious feature is that at a later date the stump may undergo similar changes, and so also even the stump after a still higher operation.

The affected part is often hot and apparently well supplied with blood and the onset of gangrene is thus puzzling and paradoxical. Several explanations have been advanced, but certainly important precipitating causes of circulatory deficiency are trauma, infection and operation, in particular an ill-timed ligation of a main artery proximal to the fistulae.

The blood travelling from the heart along a main artery becomes faced with alternative routes of progression on approaching an arterio-venous fistula:- (a) it may continue the normal route along the artery, ignoring the fistula, and into the terminal branches, through the capillaries and into the veins; (b) much of it may leave the artery before reaching the fistula, and pass into the collateral circulation which may be efficient to maintain a good distal circulation: (c) it may take the abnormal route from the artery through the fistula directly into the veins. The last path, however, is the path of least resistance, and, depending on the size of the fistula, the amount of blood passing through it will be determined; thus the larger the fistula or the more numerous the fistulae, the greater the volume of blood. Under these circumstances, it follows that the peripheral part of the limb will not receive the full share of blood destined for it, a fact which can be confirmed by arteriography. An additional feature is that the large amount of blood entering the veins through the fistula impedes the venous return of deoxygenated blood from the distal part of the limb. Therefore, in a severe case, there are the two important factors of deficient arterial blood supply and venous congestion, which produce a state of anoxemia of the tissues distal to the fistulae and lead to the typical clinical appearances. This conception /

conception of the abnormal circulation is probably correct in most cases of fistulae.

In the case of arterio-venous fistulae of the hand, foot or digit, often designated a cirsoid aneurysm, there is tremendous dilatation of the arteries entering the part, so that there appears to be an unduly good blood supply. The tissues, however, beyond the fistulae, for example a digit, are not permitted to utilise the blood, because the greatest volume of the arterial blood passes through the fistulae into the veins.

Another suggested cause of the poor blood supply to the parts beyond the fistulae is that the sympathetic nerves may be in a state of continual irritation at the site of the fistulae, causing spasm of the main arterial trunk beyond and also of the collateral circulation. This factor is unlikely to be active when there is any dilatation of the arteries, but it probably is of importance when sudden signs of vascular insufficiency develop.

Proximal ligation of a main artery is to be condemned in arterio-venous fistulae of all types and in all situations, with the important exception of a carotid-cavernous sinus fistula. About one hundred years ago it was advised that the operation be abandoned in arterio-venous fistulae, and yet, in spite of that, it is still performed. The operation may effect transient improvement but usually is followed by a state of affairs worse than the original. At other times it may have no influence whatever in the fistulae beyond. Of greatest importance is the fact that it is very liable to precipitate the onset of gangrene, even in a limb where the circulation was previously fairly adequate. Reid (76) quoted the remarks of Horner in 1841:- "Did not mortification ensue from its being "easier, on a ligature being applied to the femoral "artery, for arterial blood to flow by the anastomoses "of the obturator, gluteal or ischiatic arteries into "the circumflex, thence into the sac and return thence "by the femoral vein, than to flow to the foot and the "parts below the groin". This explanation, though applied to traumatic cases, is equally applicable to congenital cases. Perusal of the literature reveals how many cases have required amputation for gangrene following the operation. In some cases, however, it may be justifiable to attempt the operation if it is obvious that no local attack on the fistulae is possible nor any other treatment is likely to be of avail.

Rarer causes of the onset of gangrene are the rupture of a tortuous, dilated artery proximal to the fistulae, and the detachment of an embolus from such an artery and its lodgment more distally.

S E C T I O N E I G H T.

DISCUSSION on PATHOLOGY and ETIOLOGY (Contd.)

THE SIZE of the BONES.

Variations.

The peculiar variations in the size of the bones in any of the congenital vascular lesions have already been studied in detail in Section Four. They may co-exist with actual pathological changes in the bone or either may occur independently. Reference will be made chiefly to the limbs, for the sake of clarity, although the skull, jaws and trunk may be similarly involved.

Vascular Influences in the Normal Growth of Bone.

The exact details of the normal growth of bone are by no means well understood and there has been much controversy as to the roles played by the osteoblast, the periosteum and vascular influences. It is generally admitted that bone growth is a complex process of simultaneous accretion and absorption, but there is no intention of discussing the several disputed factors. It is necessary, however, to refer briefly to vascular influences, as they are believed by many authorities to be responsible for the changes in size in congenital vascular lesions.

The views of Leriche and Policard, while at variance with older theories, have received much support, notably by Greig (198) and Watson Jones and Roberts (199). According to them, an increase in arterial blood supply gives rise to decalcification and a decrease to sclerosis. The main features are that these processes are phenomena controlled by circulatory variations independent of cellular action, and that the arteries seem to determine absorption rather than building of bone.

Brash (129) made important observations on the growth of normal bone, but disagreed with the views of Leriche and Policard. He could not believe in a doctrine which ascribes absorption to a hyperemic activity of the circulation, and accretion, with its marvellous results in the building up of bones, to an ischaemic sluggishness of the circulation. He also dismissed as unsatisfactory the suggestion that the sympathetic control of blood vessels is important during the growth of bone. He considered it more likely that, in the matter of normal growth, the rate of blood flow is itself controlled in relation to the requirements /

requirements of accretion or absorption of osseous tissue determined in other ways. He asked if it is not more probable that the agency of cells is in some way directly responsible rather than mere variations in the supply of blood.

The Effects of an Increased Arterial Blood Supply.

The most general tendency, though not necessarily correct, in congenital vascular lesions is to ascribe to arterial hyperemia the production of hypertrophy of the bones and also of the soft parts. On account of the excessive vascularity so often encountered in a limb, Horton (92) believed that an increased flow of arterial blood to the bone itself is the basis of the hypertrophy. Horton and Ghormley (94), from a study of arteriograms, came to the conclusion that, when there is an increase in the length of a bone, arterio-venous fistulae are adjacent to the epiphyseal line, but that, when there is no increase in size, the fistulae are along the shaft of the bone. Thus they maintained that the vascularity in the region of arterio-venous fistulae allows an increased supply of arterial blood to the adjacent bone, which stimulates bony growth and gives rise to the enlargement.

This view, however, although simple and attractive, is open to serious criticisms. The hypertrophy, as previously noted, frequently involves every bone of a limb, and it seems most unlikely that arterio-venous fistulae can be situated, without exception, in the region of all the epiphyseal lines. Some examples of marked hypertrophy of a limb are found with only slight or no arterial hyperemia, as in minor degrees of arterio-venous fistulae or in true phlebectasis, and, conversely, there may be an absence of any hypertrophy in spite of considerable arterial hyperemia. There is, however, little proof that arterial hyperemia, if it does exist, is ever really beneficial, because in spite of it, signs of circulatory insufficiency may be present. Investigations in arterio-venous fistulae rather indicate that the increased amount of blood flowing in the arteries tends to pass largely through the fistulae and does not reach the capillaries, so that the bones are not directly influenced by it.

The Effects of Venous Stasis.

As distinct from arterial hyperemia, the effects of venous stasis or passive hyperemia have been studied, particularly by Pearse and Morton (145). They suggested that venous stasis stimulates the growth of bone and also accelerates the healing of fractures. An increase in length and thickness of bones can be produced by various conditions giving rise /

rise to venous congestion, such as arterio-venous aneurysm, angiectasis, varicose veins, long continued inflammation and irritation of the periosteum. Studies in the blood changes in venous stasis reveal an increase in the volume of the formed elements, an increase in the total plasma protein, an elevation of the oxygen capacity and of the carbon dioxide content, and a fall of the pH causing a relative acidity. It is possible also that ergosterol-like substances are increased and that concentrations in the region of a bone injury may accelerate repair. Another possibility is that the solubility of calcium is markedly altered by minute amounts of iron, which is known to be deposited in chronic venous congestion.

McMaster and Roome (130), in an experimental study on dogs, found that venous stasis hastens repair. In conditions which produce venous stasis, including haemangiomata, there are all stages of congestion from a sluggish circulation to marked venous stasis. These authors believed that bones grow more rapidly and heal more promptly in the presence of venous congestion.

Venous stasis must be reckoned as an important possible cause of the bony hypertrophy in congenital vascular anomalies. It is observed most obviously in cavernous haemangiomata, in phlebectasis and in slight cases of arterio-venous fistulae. It is, however, noted in the more severe cases of arterio-venous fistulae, when the entry of arterial blood into the venous system hinders the adequate return of venous blood from the tissues more distal and thus produces venous congestion of those parts. The influence of venous congestion can thus be effective at a considerable distance distal to the fistulae and it is not necessary to postulate arterio-venous fistulae in the vicinity of all the epiphyseal lines in a case of uniform hypertrophy. The patchy type of hypertrophy, for example of isolated digits, can be more constantly and easily explained by variations in the degree of venous congestion than by local alterations in the arterial blood supply.

It is necessary to explain the rare occurrence of underdevelopment of a limb in the presence of venous congestion, Reid (76) recording such in a case of a venous haemangioma. It is possible that the overdevelopment of veins may be so extensive as to interfere seriously with the architecture of the bone, and thus the actual effect of the venous congestion is countered. Pathological changes of such a nature in bone will be discussed later. It is to be noted also, that the limb may be underdeveloped, in spite of venous congestion, owing to an entirely different concomitant cause /

cause such as previous poliomyelitis or radiotherapy.

The Influence of the Sympathetic Nerves.

Conflicting evidence has been produced on the action of the sympathetic nerves on the circulation in cases of arterio-venous fistulae and also in cases of abnormal bony growth, whether or not associated with such fistulae.

In Section Seven, the suggestion was noted that a decrease in the sympathetic tone of the whole limb results in an increased vascularity which in turn accounts for the increase in size. Reference was also made to the opposite view that, owing to sympathetic overactivity, there is spasm of the vessels at the site of arterio-venous fistulae and also of the collateral vessels thereby impairing the distal circulation.

Harris, K.E. and Wright, G.P. (32) gave an account of a case of haemangiectatic hypertrophy of a limb, which appears to have been an excellent example of arterio-venous fistulae, although not so diagnosed. In experiments on kittens, they showed quite definitely that destruction of the sympathetic innervation to the fore-limb causes an increased blood supply but results in no increase in the length of the bony structures. It was thought possible that the destruction of these nerves has little or no influence upon the nutrient arteries to bones and epiphyses because their encasement in a rigid structure makes dilatation difficult or impossible.

McMaster and Roome (130), continuing the experiments already mentioned, noted that, after a lumbar sympathectomy, there is an arterial hyperemia with an increased blood flow and without venous stasis or sluggishness of the circulation. Consequently this procedure is not to be expected to have the same stimulating influence on bone growth or repair as venous ligation.

Harris, R.I. and McDonald (128) produced completely contrary evidence. The chief work was on lower limbs previously paralysed by anterior poliomyelitis, but they also mentioned the causes of overgrowth of a limb in growing children and included arterio-venous aneurysm and haemangioma. They concluded that a prolonged increase in the blood supply to the lower limb of a growing child can result in acceleration of the rate of growth, lumbar sympathectomy being a method of inducing this.

The Effects of an Increased Temperature and other Suggested Factors.

Chandler /

Chandler (62) believed that alterations in the rate of growth may be due to the increased circulation of inter-cellular fluid or to the increased temperature. Harris, K.E. and Wright, G.P. (32), besides the observations already noted, suggested that a raised temperature, so often demonstrated on the skin, may itself be a stimulus to increased growth of bony and soft tissues. Paterson and Wylie (26) were of the opinion that the hypertrophy of the lower limb in the case reported by them was best explained by the increased vascularity and heat around the knee joint at the growing ends of the femur and tibia.

Zondek (225), while admitting that the problem is not settled, suggested that localised overgrowth may be regarded as localised acromegaly or gigantism. It is feasible, therefore, that a vascular anomaly may permit a high local concentration of the growth hormone of the anterior lobe of the pituitary.

Klippel and Trenaunay (11), in describing the syndrome of naevi, varicosities and hypertrophy, did not hesitate in considering it the result of a single congenital abnormality, with no question of a pathological coincidence. The impression was that the bony hypertrophy is not due to the vascular abnormalities but is an associated lesion.

In animal experiments, Wu and Miltner (131) observed that stimulation of growth in length was produced by the simple procedure of loosening or stripping periosteum from the shaft of the bone but no definite explanation was offered.

The Influence of Disuse.

Disuse, although playing no part in hypertrophy, may be of importance in the less common atrophy or stunting of bone and soft tissues in vascular abnormalities. It is possible that, on account of its abnormality, the limb is not such a useful member as the opposite limb and consequently falls into a state of relative disuse. This factor of disuse was stressed by Harris, R.I. and McDonald (128) in their work on paralysis due to poliomyelitis. They stated that the shortening is due to the loss of accessory factors which normally enhance the basic growth rate at the epiphyseal line, these known factors being the contractions of normal muscles and the maintenance of a normal blood supply. Such factors may similarly be deficient in vascular abnormalities, as the result of disuse. Pure disuse atrophy, however, is liable to be a complication of actual pathological changes in the bones, as will be discussed subsequently.

The Effects of Radio Therapy.

The treatment of haemangiomata by X-Rays or radium /

radium is important as it may ultimately give rise to a profound disorder of the growth of bone, as well illustrated in Cases Seven and Eight. The presence of stunting in vascular abnormalities may at first sight be deceptive unless the history of previous irradiation is available. When applied to the growing end of long bones, irradiation produces considerable destruction of the cells of the epiphyseal cartilage, so that, depending on the intensity of the irradiation, partial or complete arrest of growth results at that site. The planned therapeutic uses will be discussed in a later section, but mention is now made of certain clinical and experimental studies on the stunting produced.

Ward and Horton (98), in case 34 of their series, described the enlargement of a lower limb associated with arterio-venous fistulae in a child. X-Ray treatment produced improvement of the vascular anomaly, but thirteen years later the limb was 3 cms shorter than the opposite limb.

Bisgard and Hunt (140) described the effects on two clinical cases. In the first, radium had been applied over a naevus on the finger of a child of three, but two years later the finger had failed to lengthen. In the other, a tumour on the medial side of the knee was irradiated with both radium and X-Rays, and ultimately there appeared a genu varum deformity, an early closure of the medial side of the epiphyseal line and a marked shortening. The authors also carried out experimental studies, among their conclusions being (a) that the shaft of a long bone can be irradiated without causing a disturbance of growth, provided the epiphyseal cartilages are protected from the direct action of the rays, and (b) that the action of X-Rays on the epiphyseal cartilage cells is solely destructive and produces premature termination of growth.

Regen and Wilkins (141) also showed that large doses of X-Rays to the fore-limbs of growing rabbits completely stopped further growth of these limbs. Evidence of a similar nature was advanced by Engel (144) using radium, and by Barr, Lingley and Gall (142) using X-Rays.

Comment.

In the face of conflicting views on the process of the normal growth of bone, it is not possible to be accurate on the causation of bony changes in congenital vascular lesions. In the case of abnormal bony development in these lesions, it may well be that the effects of vascular influences havebeen over-emphasised. It seems reasonable, as suggested by Klippel and Trenaunay, that the bony changes are not secondary /

secondary to the vascular influences directly, but that both are due to a common fundamental error in development. In favour of this view is the fact that the hypertrophy may be present in infancy before the vascular changes have become prominent enough to account for it fully.

Carleton, Elkington, Greenfield and Robb-Smith (201), while reporting the rare Maffucci's syndrome, to be discussed later, gave some general views on the simultaneous occurrence of two abnormalities in the same individual. The possible explanations were:- (1) an accidental association (improbable); (2) the multiple effects of a single gene; (3) linkage. i.e. the immediate proximity on a chromosome of two genes, each responsible for one of the abnormalities; (4) the co-operating or inhibiting action of other genes, serving either to heighten the effect of a main gene or to diminish, mask or even alter its effect; (5) the co-operation of a single gene and an environmental factor. No dogmatic opinion was expressed in view of the obvious inadequate knowledge of the subject. It was maintained, however, that the different anomalies are coincidental rather than consequential, a view which must command considerable agreement.

Of the possible vascular influences, venous stasis has most to commend it, as it may be present in any type of vascular anomaly, regardless of the presence or absence of arterio-venous fistulae, and as its effects are known to encourage an increase in the size of the bones. Arterial hyperemia, although it has received much support, cannot account for the same bony changes occurring in the absence of arterio-venous fistulae. In a case where it is marked, as in a cirsoid aneurysm, decalcification rather than hypertrophy is the rule. It is of interest to note that traumatic arterio-venous fistula in a child may result in an increased size of the affected limb. An arterial hyperemia then exists only in the immediate vicinity of the fistula, and the predominant features distal to it are venous congestion and an impaired flow of arterial blood.

The increased temperature often found in vascular abnormalities is probably of importance, as it occurs both in the presence and in the absence of arterio-venous fistulae. It seems that cellular growth may be stimulated by it and form an adequate reason for the hypertrophy.

There is no uniformity of opinion as to the actions of the sympathetic nerves supplying the part, but the various suggestions have been quoted. The view that a destruction of the nerves produces hypertrophy, assumes arterial hyperemia to be the active influence and is thus open to the same criticisms.

PATHOLOGICAL CHANGES IN BONE.

Variations.

Apart altogether from alterations in size, several different pathological appearances may occur, some due entirely to variations in the local blood supply, some to an abnormal development of the vessels and others to an angiomatous tumour, an accurate line of demarcation being impossible. The bony lesions chiefly to be discussed are those found in association with vascular abnormalities in the overlying soft tissues, but mention will also be made of apparently independent lesions. Among other items, an account will be given of the rare Maffucci's syndrome of haemangiomata and dyschondroplasia.

Osteoporosis.

The simplest degree of pathological change is the intense osteoporosis or decalcification found in the vicinity of a cirsoid aneurysm and any other active arterio-venous fistulae, which are usually in the soft tissues but may be located in a bone. This osteoporosis affects bones previously and otherwise quite normal, and is due to loss of calcium from them. It is the consequence of the hyperemia induced around arteriovenous fistulae, and it does support the teaching of Leriche and Policard that hyperemia gives rise to osteoporosis. It is also a strong argument against the view that this hyperemia is the cause of hypertrophy of bones.

Case Five of my series demonstrated arteriovenous fistulae in the bone and soft tissues of the second toe, associated with intense vascularity of the whole foot, the result being that all the other bones in the foot showed extreme osteoporosis. Reports of similar examples of osteoporosis are given by Gilmour and Bolam (60), Bernheim (25), Alajouanine, Thurel and Hornet (54), Freund (56), and Horton (92).

The term atrophy of bone is unfortunately used by some authors as being synonymous with osteoporosis. It should strictly be applied to a decrease in size only, thus being the opposite term to hypertrophy, and it is used in this sense in this discussion.

Enlarged Vascular Channels in Bone.

This type of change is a common manifestation of congenital vascular abnormalities and it may be associated with osteoporosis. The nutrient foramina alone may be enlarged or many large abnormal foramina may exist, transmitting either arteries or veins. In the more extreme case, the bone appears to be riddled with /

with such openings and it then contains large blood sinuses through which arterial blood passes directly into veins. Reid (72) described in Case 31 the examination of an amputated tibia in which arteries and veins passed through large openings in the cortex and in the interior of which were large vascular cavities connecting witharteries and veins; there was no sign of a tumour growth. Lewis, D. (41) described many large vessels perforating the radius in Case One of his series and he also quoted Gross's findings of communications between arteries and veins of the tibia and fibula. Adams (2) showed arterio-venous anastomoses within the calcaneus, and Wright, L.T. and Logan (90) demonstrated the presence in the bones of large nutrient foramina and vacuoles, along with osteoporosis. Patel (37) reported a cirsoid aneurysm of the scalp with numerous vascular openings in the cranium.

In some cases of this nature, the actual arterio-venous communications are located within the bone, whereas in others the abnormal channels are purely or largely venous, without any notable increase in the arterial supply. Lesions of this nature may be localised to part of one bone, when they are most liable to be considered tumours, or they may affect one entire bone or several bones of a limb.

In my own series, judging from X-Ray examination, Cases Two, Seven and Eight demonstrated numerous enlarged vascular channels, along with osteoporosis and atrophy, while Case Six was probably similar.

The cause of these abnormal channels is in dispute and several possibilities may be considered. Lesions in the bone and adjacent soft tissues may be present at birth, both due to the same vascular anomaly. The vascular channels in the bone may then increase in size and number in subsequent years due to the same mechanical effects of an abnormal circulation as already described in Section Seven. At other times, in association with a soft tissue anomaly, the bone at first may be normal but later may become osteoporotic and penetrated by abnormal vascular channels. The osteoporosis can be explained by the increased vascularity in the neighbourhood and the penetration of blood vessels can again be ascribed to the mechanical effects of the circulation. This finding is most common in relation to a cirsoid aneurysm.

On the other hand, it is maintained by some authorities that the essential lesionmay be a vascular tumour of the soft tissues, which secondarily invades bone and causes it to become permeated by the tumour. The further possibility of the enlarged vessels being caused /

caused by a primary bone tumour will be considered immediately.

Haemangioma of Bone.

This is not an accurately defined lesion and it may occur in the presence or in the absence of a soft tissue vascular lesion. The term is given both to the state produced by enlarged vascular channels and also to true primary tumours; most of the debatable points discussed with the soft tissue vascular lesions are applicable here also.

The widespread type of lesion involving several bones, as in Case Seven, is usually due to a vascular abnormality with associated soft tissue changes, but it is not a true neoplasm. However, Ackermann and Hart (203) reported a case of multiple primary haemangiomata of the bones of a lower limb, which were understood to be tumours and were not associated with soft tissue lesions. The subject of multiple lesions, including those in bone, will be discussed in Section Nine.

It is the solitary type of haemangioma which may give rise to more difficulty in diagnosis and is more debatable. Bucy (135) gave a most useful review of haemangioma of bone, and recorded cases numbering thirteen in the skull, twelve in the vertebrae and fourteen in other bones. To the naked eye, the lesion consists of numerous fine bony trabeculae and is intensely vascular. Microscopically, the tissue between the trabeculae is composed of large cavernous spaces containing blood cells and lined with a layer of flat endothelium. Bucy was unable to decide whether these lesions are neoplasms or vascular malformations.

Geschickter and Maseritz (139) added sixteen more cases of proved haemangioma, and also one doubtful case of angioma of the skin, with a suggestion of possible secondary involvement of the long bones of a limb. Anspach (138) mentioned that although a primary haemangioma is favoured by some as the essential lesion, yet others maintain that a large soft tissue haemangioma is apt to erode bone, leaving a smooth edged filling defect.

Nemenov (83) believed the condition to be a true tumour of bone, and Ewing (168) described it as a multicystic expansive tumour. Hitzrot (137), often quoted, reported a case of haemangioma cavernosum of the humerus, in which, however, the findings did not appear to be convincing and might well have been the result of trauma or a bone cyst. Ballance, Sir H. and Shattock (134) also described an isolated lesion in /

in bone with a histological diagnosis of a very rare capillary haemangioma, no evidence of sarcoma being present.

Reid (73) quoted a report by Carnier and Ranvel on angioma of bone:- the tissue is hollowed out into alveoli, communicating in an irregular manner with each other; blood circulates in this cavernous system, which occupies the place of the capillary system, situated as it is between arteries and veins; the circulation is active; there is no suggestion of any actual tumour growth.

The diagnosis of such lesions is not easy and certain other bony conditions may produce similar local appearances, especially a giant cell tumour, cystic diseases, and sarcomata, notably an angio-endothelioma, in which there is an extensive formation of blood vessels.

In Case Three of my series, the lesion in the lower end of the femur was characteristic radiologically of a haemangioma of bone. The extensive vascular anomaly in the limb and the operative findings furnished strong evidence that the lesion was not a tumour, but was a vascular malformation, composed of large cavernous spaces through which arterial blood passed directly into the venous stream.

Case Five demonstrated a similar type of localised lesion in the first phalanx of the second toe, which was cyst-like on X-Ray examination and was quite different from the generalised osteoporosis of the foot. Here it appeared that arterio-venous fistulae were present both in the bone and in the soft tissues of the toe, which was the centre of a most profound vascular disturbance. Though this type of bony lesion is also designated as a tumour, there was no evidence of a neoplasm. Similar examples have been reported by Ward, C.E. and Horton (98) case 20, by Horton (92) case 2, and Horton and Ghormley (95) case 1.

Periostitis and Destructive Arthritis.

The former was reported by Bell and Inglis (27) in the fibula and by Gilmour and Bolam (60) in the toe in case one. The latter may cause ankylosis of one or more joints, Pemberton J. and Saint (35) demonstrating the change in case three in the wrist and hand and in case five in the finger, and Horton (92) in case five in the knee and ankle. Though not producing ankylosis, it was present in Case Eight of my series.

Pathological Fracture.

This /

This may occur as a complication of the bone lesions already mentioned. Couch (53) had an example of fractures of both bones of the forearm which surprisingly united without difficulty, and Nemenov (83) described a case where several fractures of the forearm had occurred at different times, much deformity resulting. Non-union of fractures of both bones of the forearm was reported by Lereboullet and Petit, quoted by Weber (116), and non-union of a fractured femur took place in Case Two of my series.

Fibrous Dysplasia.

There is a rare type of dysplasia of bone, known as polyostotic fibrous dysplasia when mild, and as Albright's disease when more severe, in which there is a combination of a bony lesion akin to osteitis fibrosa cystica with endocrine disorders and cutaneous pigmentation. The subject was carefully reviewed by Falconer and Cope (200) who considered it to be due to a congenital disorder of development. Though beyond the scope of the thesis, it is of interest to recall that Stauffer, Arbuckle and Aegerter (100) described such a case in which a congenital arterio-venous aneurysm was present. It was probable that the various features were evidence of different errors in development arising simultaneously but that one error was not necessarily an effect of another.

Dyschondroplasia and Haemangiomata.

Under the title of Maffucci's syndrome, Carleton, Elkington, Greenfield and Robb-Smith (201) gave a most detailed account of a congenital morphological anomaly, in which dyschondroplasia, a defect in cartilage bone formation, is associated with vascular hamartomata. The bony lesion is characterised by irregular modelling of the bones, large chondromata with a tendency to malignancy and situated near the epiphyseal lines, uneven development on the two sides, and perhaps dwarfing or deformity. The hands and feet in particular may become seriously involved and transformed into huge masses of cartilaginous tumour growth. The vascular lesion takes the form of dilated veins, localised soft bluish venous dilatations and telangiectases; phleboliths are also a feature.

The authors quoted eighteen previously recorded cases of this nature, the first being that of Maffucci in 1881, and they also referred to four other doubtful cases. They gave full reports of two personal cases, in the first of which it was suggested that certain of the vascular lesions were arterio-venous anastomoses with histological appearances reminiscent of the glomoid anastomosis. Of interest in connection with the views already discussed earlier in this section /

section was their opinion that the bony and the vascular lesions are coincidental rather than consequential, and that the vascular anomalies do not induce the bony changes. It was thought possible that the syndrome is consequent on a foetal neurotrophic disturbance and belongs to a group of congenital mesodermic dysplasias.

No case of this nature occurred in my personal series of cases, but it is obvious that there is a considerable resemblance between Maffucci's syndrome and the vascular anomalies under discussion, the bony lesions being the chief difference. If it were not for the absence of chondromata, however, the diagnosis of the former condition would have required serious consideration in Cases Two, Seven and Eight.

Glomangioma.

This subject will be discussed independently in Section Ten. Seeger (78) mentioned that normal arterio-venous anastomoses are common within the digital bones and Bergstrand (204) reported several glomangiomata within the tarsal bones.

INVOLVEMENT OF MUSCLE.

As with vascular lesions in other situations, there is evidence of the same controversy about either an anomaly or a tumour being the cause. A haemangioma of muscle has been described, sometimes in large series, by several authors, notably Davis (13a) and Davis and Kitlowski (13b), and also Jenkins and Delaney (165), Ewing (168) and Kidner (59). There was seldom any proof that these lesions were tumours, the histological appearances being chiefly large blood spaces and vessels, although endothelial proliferation was demonstrated on occasion.

It is an unfortunate misconception that leads to the classification of angiomata as occurring in a specialised tissue like muscle, as practically always there are extensive changes elsewhere. There is no doubt that in any of the vascular anomalies, the muscular tissue may become atrophied and replaced widely by greatly dilated veins. Another type of muscular lesion is the occurrence of localised honeycombed masses in several muscles, with the structure of smaller vessels and spaces and certainly not due to a tumour growth.

Quoting from my personal series, Case Seven showed extensive generalised&localised involvement of muscle with no evidence of a primary tumour of muscle, and in Case Eight, although the muscular tissues were largely /

largely replaced by blood vessels, a histological appearance of normal veins was present. Under such circumstances, it would have been quite incorrect to make a diagnosis of angioma of muscle, and yet that has been done in many reported cases.

INVOLVEMENT OF PERIPHERAL NERVE.

The above remarks are also largely applicable to the occurrence of so-called angiomata in the peripheral nerves. Stewart and Bettin (24), and Reichel quoted by Freund (56) described such examples, and Case Seven of my series demonstrated a widespread vascular infiltration of the brachial plexus, without there being any suggestion that the lesion was primarily in a nerve. Love and Horton (222) described the production of ulnar nerve paralysis by arterio-venous fistulae.

CHANGES IN THE SIZE OF THE CARTILAGE OF THE AURICLE.

In the report on Case Twelve, there was raised the debatable subject of the causation of the considerable hypertrophy of the cartilage of the auricle. The nutrition of cartilage under normal circumstances has received little enough attention in the literature and it has not been possible to trace any satisfactory reference to factors influencing the abnormal growth of the auricular cartilage. Several factors will now be examined and some personal opinions will be advanced.

It is necessary to recall the fact that cartilage is an avascular structure, which does not derive its nutrition directly from blood which has passed into capillaries. Instead, it is believed that the nutrition is obtained from lymph which circulates in lymphatic plexuses related to the perichondrium, but it is not certain if actual lymph channels exist between the cartilage cells.

In conformity with the commonly stated, though probably not correct, view on hypertrophy of bone, the first impression, on examining a case such as the one reported, is that the increased amount of blood entering the tissues of the ear is responsible for the hypertrophy of the cartilage. In view of the avascular nature of cartilage, however, there is no justification for the theory that the cartilage cells obtain an extra nutrition from the increased amount of arterial blood.

The influence of venous stasis appears to be of greater significance and is supported by the clinical evidence of a dusky cyanosis of the affected part, although the avascular nature of cartilage is perhaps against it. A personal suggestion now advanced is that /

that the marked venous congestion is actually responsible in that it produces a state of local lymph stasis. This seems quite reasonable in view of the knowledge that cartilage derives its nutrition from lymph and that lymph stasis encourages the proliferation of connective tissue.

Both arterial hyperemia and venous congestion tend to produce an increase in the local temperature, and it is possible that this factor is of some importance, as there is experimental evidence that it stimulates cellular proliferation in vitro.

Finally there is the possibility that the enlargement of the cartilage is not in any way secondary to the vascular abnormality but is a concomitant lesion, both being due to an error in the developing mesoderm.

SECTION NINE.

DISCUSSION on PATHOLOGY and ETIOLOGY, (Contd.)

MULTIPLE and MALIGNANT ANGIOMATOUS LESIONS.

Variations in Site and Structure.

It is evident from a study of personal and other cases that congenital vascular anomalies and haemangiomata are frequently multiple and widespread in different tissues, but there is considerable difficulty in arriving at a satisfactory explanation for such phenomena or at an adequate classification. The controversial opinions on the subject of haemangioma have already been discussed at length and Harvey, Dawson and Innes (147) very wisely point out that it is not possible to lay down where an angiectatic malformation ends and an angiomatous tumour begins. In the event of multiple lesions, even if one grants that they may be tumours, it has still to be decided whether they arise independently although simultaneously, or whether one lesion is a primary tumour and the others secondary deposits. The term benign metastasising haemangioma is sometimes applied to multiple lesions but it is a bad term and one better avoided. A multicentric development is probably the usual explanation, but this multiplicity is often in favour of a vascular anomaly and unlike the behaviour of a tumour. Undoubted cases of malignancy, however, are reported. A further important point is that an anomaly may simulate a malignant lesion by its rapid spread induced by purely mechanical factors. It appears, therefore, that angiomatous lesions of very varied natures do exist and an attempt will now be made to discuss the various possibilities. Multiple lesions occur more commonly than are obvious clinically and only a complete post mortem examination may reveal the unexpected. The lesions chiefly under discussion are those in the skin, subcutaneous tissues, bone, muscle and peripheral nerves, but attention will also be drawn to the coincidence of these lesions on the one hand and visceral lesions on the other. Purely visceral lesions are beyond the scope of the investigation.

Multiple Lesions with Simple Histological Structure.

Without repeating the controversial points reviewed in Section Seven, there is no doubt that the common multiple angiomata of the skin, subcutaneous tissues and mucosae have a perfectly simple histological structure /

structure of dilated vascular spaces and owe their origin to a multicentric vascular anomaly.

Of greater interest is the coincidence already noted of multiple angiomata occurring in many different tissues. Case Seven demonstrated scattered lesions in skin, subcutaneous tissue, muscle, bone, peripheral nerve, mucous membrane of pharynx and aesophagus, and pericardium; there was also an abnormal cerebral vascular arrangement. Among similar examples in the literature, Jaffé (169) reported the case of an infant in whom the post mortem findings included multiple haemangiomata, of a simple histological structure, in the skin, cerebral and spinal meninges, anterior roots of cervical nerves, diplöe, thyroid, lungs, intestine and spleen. He also quoted several other examples, the authors and sites alone being stated:- Billroth - skin, liver, spleen and bones of skull; Gascoyen - skin, liver, parotid and intestine; Ghon - skin, mucosae, mesentery and retroperitoneal tissues; von Rokitansky - skin, epicardium, pleura, peritoneum and choroid plexus; Runge - skin, mucosae, liver and heart; Topfer (case 1) - skin, mucosae, submaxillary gland, thyroid, liver, lung, intestine and bladder; Topfer (case 2) - skin, mucosae, mediastinum, pericardium, liver and kidney; Ullmann - skin, mucosae, peritoneum and liver.

Parsons and Ebbs (173) gave a long account of a most unusual case of generalised angiomatosis with storage reticulosis, which on clinical examination showed evidence of the osseous form of Gaucher's disease. At post mortem examination, there were found cavernous haemangiomata in the liver, spleen, retroperitoneal glands, thymus, mediastinum, lungs, pleura, kidney and most of the bones.

In all these cases mentioned, the histological picture was chiefly that of simple vascular spaces and the origin was believed to be a multicentric development, with no suggestion of one primary tumour and multiple secondary deposits.

A point of doubtful significance is illustrated by the participation of serous membranes in some of the above cases. Harvey, Dawson and Innes (147), under the heading of endothelioma, included the angiomatous lesions arising from vasoformative cells and the lesions arising from membranoformative cells of the serous and synovial type. In the case of Parsons and Ebbs, there was a very widespread involvement of all reticulo-endothelial tissues as well as the angiomata. It seems, therefore, that in certain rare circumstances there may be an extensive aberration of endothelial cells in general.

An example of a coincidence of simple angiomatous lesions of a rather different nature is provided by the case of Watson and McCarthy (164) of a vascular anomaly of the lower limb and a perithelial angioma of the kidney.

Multiple Simple Lesions with Cellular Proliferation.

This group is not well defined, but several examples have been recorded of multiple angiomatous lesions with cellular proliferation but no evidence of malignancy. This type is probably due to tumour growth in a congenital vascular malformation and probably is multicentric in origin, although, on the other hand, benign metastases are believed to occur. Shennan (202) described a case with angiomata of the skin of the temple, arm and buttock, in whom, on post mortem examination, there were angiomata in the superior mediastinum, root of lung, spleen, heart, kidney, liver and bone. He also quoted Borrmann's case of an angioma beneath the skin of the breast with metastatic deposits of a simple nature. Ewing (168) reported a case of multiple angiomata in the breast, mucosae, lungs and skin. Jaffé (169) mentioned other examples.

A Benign Lesion and Malignant Metastases.

Robinson and Castleman (174) described an unusual case of angioma of the breast with benign histological characteristics which produced definitely malignant metastases. The so called "benign" character must be questioned. Ward, G.E. and Jonas (71) considered a case of theirs to be of the same category, but in my opinion it bears more resemblance to the next group.

Invasive or Malignant Development in Arterio-Venous Fistulae.

The case reported first by Pemberton, J. and Saint (35) and later by Matas (36a) has already been discussed in detail in Section Seven. Here there was the definite anomaly of arterio-venous fistulae in which developed an invasive spreading tumour, without histological evidence of malignancy. Ward, C.E. and Horton (98), in Case Thirty Five, described a vascular anomaly, probably arterio-venous fistulae, of the lower limb, in which a malignant neoplasm developed, eventually causing death from widespread metastases. The clinical history was incomplete and no histological reports were published. Though the tumour was probably angiomatous, it is just possible that it may have been a melanoma or that it was due to malignant change induced by previous faulty irradiation with radium and X-Rays. The case of Ward, G.E. and Jonas was that of a cavernous haemangioma of the palm of the hand, which had /

had a definite arterial pulsation, was connected to an ulnar artery twice the normal size and from its description was possibly an arterio-venous malformation. Eventual autopsy specimens showed replacement of the epitrochlear and axillary glands by solid tumour cells and erosion of a metacarpal by a hard tumour. One possible fallacy was the presence of an adenocarcinoma of the gall bladder and adjacent lymph nodes.

A Primary Malignant Tumour and Metastases.

Many types of sarcoma are intensely vascular and may be given the prefix angio-. In spite of that they are seldom true angiomata and the vascular over-development is purely a secondary change induced by the tumour. True sarcomatous angiomata, however, are occasionally described and Jaffé (169) mentioned a few examples of vascular tumours with a sarcomatous stroma.

Kaposi's Multiple Haemorrhagic Sarcoma.

Of a different nature from other sarcomata, the rare Kaposi tumour tends to involve one extremity first but later becomes bilateral and symmetrical. The condition is progressive over a period of years, with occasional regressions, but ultimately the viscera become involved, being a cause of death. A typical lesion takes the form of a blue, red or brown superficial plaque, and later neighbouring plaques coalesce to form a considerable swelling. There is a resemblance to haemangiomata or lymphangiomata and varicosities may be present. Three stages have been described, the inflammatory, the granulomatous and the neoplastic. The pathogenesis is obscure, though it has been suggested to arise in the complex neurovascular annexes of the skin. It is, however, multicentric in origin, and the many skin lesions are not metastatic. There is no reason to believe that it is congenital in origin. A full account of the condition has been given by Oughterson and Tennant (171).

Lindau's Disease.

This disease, which appears to be a separate, rare entity, is a form of multiple angiomatosis and is a multicentric development which is not malignant. It takes the form of multiple cystic angiomata of the cerebellum, spinal cord, retina, pancreas and kidney.

De Morgan's Spots.

This is another type of multiple angiomata of the skin, which are of a perfectly simple nature. They are mentioned in Section Four on page 129.

Rendu /

Rendu-Osler-Weber Disease.

This form of telangiectases, also mentioned in Section Four on page 129, was well described by Parkes Weber (115). It takes the form of multiple hereditary developmental angiomata of the skin and mucous membranes, haemorrhage from the nose being a common feature. It is not a tumour growth but is a late developmental condition, affecting and being transmitted by both sexes. There is no haemophilia nor any diminution of blood coagulability.

Sturge-Weber Disease.

This condition will be discussed separately in this section. Though characterised by independent angiomatous lesions, there is no question of any metastases or malignancy.

Glomangioma.

Though most commonly a single lesion, it may at times be multiple, in which case it is another example of multicentric development of angiomata. It will be discussed independently in Section Ten.

ASSOCIATED INTRA-CRANIAL VASCULAR ABNORMALITIES.

The scope of the thesis does not include a study of intra-cranial vascular anomalies and tumours, but, owing to the occurrence of cerebral complications in Case Seven, it has been necessary to make a brief reference to them and to their association with extra-cranial lesions. Various degrees of abnormality are known, and in Section Seven on page 169 reference was made to the classifications of angiomatous lesions suggested by Cushing and Bailey (170) and by Northfield (126), and also to the report by Reid (72) of a case of congenital carotid-cavernous sinus fistula.

Of greater interest in the present discussion is the condition perhaps best known as the Sturge-Weber disease or syndrome, but also associated with the names of Kalischer and Dimitri, among others. As described by Parkes Weber (118) and also by Nussey and Miller (125), there is the association of an extensive cutaneous haemangioma in the area supplied by the trigeminal nerve, and a diffuse leptomeningeal haemangioma on the same side, containing calcareous deposits visible on X-Ray examination. Buphthalmia is generally present on the same side and other effects include mental defect, a contralateral hemiplegia and fits.

Rarely the Sturge-Weber syndrome and a vascular anomaly /

anomaly of a limb occur simultaneously. Newson (80) reported a case presenting the typical features of the Sturge-Weber syndrome and of arterio-venous fistulae of an upper limb. Northfield (126) gave details of a similar type of cerebral and facial lesion, associated with angiomata of the lower limb and abdominal wall.

ASSOCIATED LYMPHATIC ABNORMALITIES.

Lymphatic abnormalities and tumours may exist in the same way as the blood vascular lesions. A lymphangioma may produce a localised swelling similar to a haemangioma, and it also has a doubtful pathology, being considered either a true tumour or an abnormality in the development of the lymphatic system. Congenital hypertrophy or elephantiasis of a part or whole of a limb may be associated with or due to an abnormal development of the lymphatics, without any blood vascular lesion being present. Desaive (143), for example, described a case of widespread lymphangiomata with great enlargement of a lower limb.

As mentioned in Section Six, Chandler (62) indicated that an error in the development of the vascular tree in the fourth week of embryonic life produces a blood vessel anomaly, whereas in the sixth to eighth weeks it causes a lymphatic anomaly. Should the error persist throughout both periods, a combined blood vessel and lymphatic anomaly results, and Chandler himself reported one case in which there existed hypertrophy of both lower limbs, haemangiomata and lymphangiomata. Similar cases were those of Friedberg (quoted by Finlayson (7)), Dent (14) and Watson and McCarthy (164).

In some other examples, it has been noted that watery fluid may discharge from the skin. Thus, Pautrier and Lang (65) demonstrated how a watery blood stained fluid was derived from many small lymphangiomata, in the presence of a widespread blood vessel anomaly. Watkins (102) described an unusual example of arterio-venous anastomoses in which a transient milky discharge took place from the groin, the fluid containing many lymphocytes and being suggested to be derived from a lymphangiectasis. Shumacker (112) reported a combined anomaly with elephantiasis, in which large quantities of clear fluid discharged from the skin.

S E C T I O N T E N.

THE NORMAL ARTERIO-VENOUS ANASTOMOSIS AND ITS ABNORMALITY.

THE NEURO-MYO-ARTERIAL GLOMUS.

History.

According to Franklin (124), arterio-venous anastomoses were suspected as long ago as 1707, and Krogh (162) noted that for many years reference had been made to the existence of "derivating channels" represented by small arteries opening into somewhat larger veins. Sucquet in 1862 described peculiar vessels in the palm and sole which appeared larger than ordinary capillaries and opened directly into neighbouring veins without forming a capillary network. To Hoyer in 1877 belongs main credit for the modern conception of these vessels, but the two names are frequently linked together in the term Sucquet-Hoyer canal, which is a part of the glomus. Interest in the glomus was roused by the work of Masson (150) on the glomus tumour and an excellent review of the subject has been given by Popoff (159); Seeger (78) has also recently referred to it in detail.

Site.

Hoyer originally demonstrated aterio-venous anastomoses in man only in the hand and foot, especially the fingers and toes, including the digital bones, and in the sex organs, but he found them in most mammals in additional sites such as the ear, tip of nose, lips and tip of tail. Popoff considered the typical sites to be the ventral and lateral parts of the digits, the nail bed and nail matrix, the thenar and hypothenar eminences and the sole near the heel. More recently it has been believed that the anastomoses are more widespread than generally stated, occurring in the cutis in many parts of the body and also in the mesentery.

Greig (154) noted the relation of the glomus to the pacinian corpuscles and other varieties of nerve endings in the skin, which are undoubtedly organs of tactile sensibility, suggesting that the regulator action of the glomus is connected with their function. Greig also asked if the glomus is the organ of Ruffini, which is a complex corpuscle, and he noted that Masson, although not claiming them to be identical, suspected them to be one and the same organ.

Anatomy /

Anatomy.

Popoff has carefully summarised the important anatomical features of the glomus, based on the original work of Masson. The entire anastomotic unit is known as the glomus or neuro-myo-arterial glomus, and the portion of channel connecting artery and vein, that is the anastomosis proper, is called the Sucquet-Hoyer canal. The glomus includes (1) an afferent artery, (2) the Sucquet-Hoyer canal, (3) neuroreticular and vascular structures around the canal, (4) outer lamellated collagenous tissue, and (5) primary collecting veins. One afferent glomic artery forms from one to four separate Sucquet-Hoyer canals, and the beginning of the canal is marked by the presence in the afferent artery of cushion-like endotheliomuscular elevations, the function of which is to direct the blood flow into the canals and the preglomic arterioles. The wall of the canal is rather thick, has a specific structure and is free from elastic tissue except for its proximal part. The canal is usually coiled and twisted, the lumen does not exceed 0.1 mm in diameter, and the average length is 0.5 - 0.8 mm. The canal is surrounded by a clear zone of a loose fine collagenous reticulum, enclosing a rich network of non-medullated nerve fibrils, which are of considerable importance in that they control the function of the Sucquet-Hoyer canal. The glomic unit is supplied with a system of preglomic arterioles, nourishing all its constituents and forming an integral part of it, and it is surrounded with coarse lamellated collagenous tissue, which separates it from the other structures of the cutis. The primary collecting veins, although lacking in musculature, are richly supplied with elastic tissue, and they collect blood both from the Sucquet-Hoyer canal and from the preglomic arterioles. They are long and wide, and encircle the glomic unit like a ruffle; they have also been described as throttle veins.

The glomic system is absent in the foetus and in the young baby. Regeneration and the development of new canals are possible at any age thereafter.

Physiology.

The contraction and dilatation of the anastomoses are under the perfect control of local and general vasomotor mechanisms. The functions of the anastomoses, in brief, are to adjust the peripheral vessels to changes caused by internal and external influences, to control the local arterial and venous pressure, and to regulate the local and general temperature. If the digits are exposed to cold, it is through the agency of the glomic system that the local temperature is maintained, and even raised, by the diverting of blood from the capillaries and rushing it through /

being Harvey, Dawson and Innes (147), Mackey and Lendrum (148), Lendrum and Mackey (149), Freundenthal, Anderson and Weber (120), Oughterson and Tennant (171), Greig (154), Stout (152), Murray and Stout (206), Weidman and Wise (151), Bailey (153), Lewis, D. and Geschickter (155), Raisman and Mayer (156), Mason and Weil (157), Adair (158), and Bergstrand (204).

Clinical Features.

The age of onset varies from childhood to old age. The majority of cases appear to be induced by trauma, a few arise spontaneously and a small number are definitely congenital. The most typical situation is beneath the nail of the fingers or toes, but the skin of the pads of the fingers and the skin of the palm are quite frequent sites. The lesion has also been shown to occur elsewhere, for example, in the forearm, arm, thigh or leg, or very rarely in the trunk or in bone. The condition is generally single, although a few cases of multiple occurrence have been recorded.

The great majority of lesions are small, varying in diameter between 3 mms. and 1 cm, a few exceed 2 cms. in diameter, and there are only a few rare instances of large size. The gross appearance depends on the site. In the nail bed, with little room for expansion, it has the form of a bluish, cellular nodule, whereas elsewhere it is quite commonly a flat, soft, bluish spot, like an isolated venous dilatation and situated in the deeper layers of the dermis. When larger, it tends to expand into the adjacent fat as a soft lobulated mass, closely resembling a localised collection of varicose veins. In any site, the lesion may increase in size on congestion, especially during a paroxysm of pain, and, following injury, bleeding may be brisk and recurrent, particularly if the overlying skin is thin and atrophic. Blood may be aspirated with ease from the larger swellings, and, though perhaps usually venous, it may be almost arterial in character as in Case Nine. On occasion, the glomangioma is pulsatile when in contact with bone and it then causes erosion of the cortex in the same way as an arterial aneurysm.

Pain is by far the most prominent symptom and it may be of terrific intensity and brought on by very slight stimulation. It has a marked tendency to radiate, so that it may spread from a tiny original focus and involve the whole limb, or even the trunk or opposite limb. It is paroxysmal in character, and it may have a severe effect on the mental health of the patient. Masson believed that the pain is caused by pressure on the adjacent pacinian corpuscles in the skin. Vasomotor phenomena may or may not be present, and /

and atrophic changes may occur in a limb either as a result of them or as a result of disuse. On rare occasions, pain may be absent or else it may develop several years after the first appearance of the lesion. Another feature may be an increase in the local skin temperature.

Pathology.

The glomangioma is composed of a tangled mass of blood vessels and spaces, and it is generally enclosed within a capsule, although occasionally it shows a progressive infiltrative growth. A vessel is lined by a single layer of flat endothelial cells, surrounded by several layers of the characteristic glomus cells. There is a supporting layer of fibrous tissue external to these cells and numerous nerve fibres are present. The glomus cells, also known as epithelioid cells, are the essential histological feature of the glomangioma, and they are the same type of cell as seen in the Sucquet-Hoyer canal of the normal arterio-venous anastomosis of the skin. Such a glomus cell is large and cuboidal or rounded, and it has a voluminous centrally placed circular nucleus, with well stained reticular chromatin. The cytoplasm is pale and sometimes vacuolated, and there is a well marked limiting membrane, as shown by Masson's trichrome stain. External to the cell there are delicate collagen fibres which separate one cell from another.

There are three principal histological variations from the typical picture of the glomangioma. (1) When the glomus cells show a predominance, there is a sheet of epithelioid cells, in which lie narrow clefts lined by endothelium (Masson's paucivascular form). (2) When connective tissue is predominant and the vascular spaces are larger, the appearances are those of a cavernous angioma, modified by the presence of glomus cells, which lie parallel to the endothelium and have a straggling continuity with the glomus cells of adjacent blood spaces. (3) If the nervous tissues proliferate, the appearances are those of a neurofibroma.

Multiple lesions are uncommon and are recognised to have independent although perhaps simultaneous origins. Like the solitary lesions, they are always simple, and without any hint of malignancy. Weidman and Wise (151) reported the case of a female in whom the first lesion became obvious at the age of fifteen, followed later by forty-eight similar lesions with the histological structure of a glomus tumour. Adair (158) demonstrated, in Case Nine of his series, four separate lesions /

lesions on the forearm, in association with a haemangioma, and Bergstrand (204) reported two cases of multiple occurrence, the bone of the foot being affected in one. Harvey, Dawson and Innes (147) quoted the case of Dott's with multiple lesions, and Case Nine of my series had four lesions. Slepyan (224) recorded a case with fourteen lesions, two of them painful.

Etiology.

Although the glomangioma is commonly referred to as a tumour, it is not certain from the writings of several authors that it is strictly a neoplasm. In the majority of cases, there is the participation, in an orderly arrangement, of the glomus cells, the connective tissue and nervous tissue, and Masson interpreted this as indicating that the origin of a glomangioma is in a hyperplasia of a normal glomus, rather than in a true neoplasm. Weidman and Wise (151) and Mason and Weil (157) agreed that the lesion is a hamartoma, and thus beyond the realm of a simple hyperplasia, but not attaining to that of neoplasia. Murray and Stout (206) believed a glomangioma to be an organoid tumour and a caricature of the normal glomus. Bailey (153) considered a glomangioma to be an overgrowth of a specific arterio-venous anastomosis and the neurones terminating in it, and to represent an organoid overgrowth, functionally as well as morphologically.

The glomangioma can form in the deeper tissues as well as in the cutaneous and subcutaneous zones of those parts of the body where no normal glomera have been identified. In noting these facts, Murray and Stout explained how the "epithelioid" cell of the glomus has been identified as the pericyte of Zimmermann, a special type of cell which wraps itself around capillaries, and, passing towards both arteries and veins, gradually merges with smooth muscle fibres. Since this cell has been demonstrated in many parts of the body, its identification offers a satisfactory explanation for the occurrence of glomus tumours in regions where the normal glomus is never found. The same authors, Stout and Murray (207), spoke also of a haemangiopericytoma as being an allied entity but separate from a glomangioma. Their work has apparently not received any great degree of support.

While most references, particularly those based on histological work, consider the glomangioma to be an independent condition, yet clinical examination tends to show how it may have an important relationship to haemangiomata and vascular anomalies, and Oughterson and Tennant (171) included it under the general title of angiomatous tumours. Several reported cases, especially those not involving the region /

region of the nail, showed merely the clinical appearances of a small localised collection of varicose veins or a venous angioma, and blood could be aspirated from them.

Considering that the glomus is a normal form of arterio-venous communication, it is surprising, as mentioned in the Comment in Case Nine, that it does not give rise more frequently to changes similar to congenital or traumatic arterio-venous fistulae. Case Nine is, therefore, probably unique in that clinical examination, including arteriography and an oxygen estimation of the venous blood, revealed arterio-venous fistulae, while histological examination showed a definite glomangioma. These findings suggest the desirability of examining large glomangiomata much more completely than in the past and it is probable that interesting information could often be obtained. The case reported by Harvey, Dawson and Innes and quoted in the account of Case Nine might possibly have shown the presence of arterio-venous fistulae. Colley (88) certainly sensed the resemblance but mentioned that the arterio-venous communication in the normal glomus is not the cause of pathological fistulae.

A further point of resemblance is that both glomangiomata and arterio-venous fistulae may be congenital or traumatic in origin, the latter being much the more common cause in both. The glomangioma also shows the same etiological difficulties as haemangiomata and is thus considered either a true tumour or a hamartoma. While it is true, therefore, that the small cellular glomangioma has the appearances of an outstanding, independent type of tumour, it is also to be noted that the larger cavernous types resemble haemangiomata, with their debatable etiology, and very rarely may assume the features of arterio-venous fistulae.

Treatment.

The treatment of glomangioma is simple and should consist of the complete local resection of the lesion. There appears to be no risk of any recurrence. While the operation can often be carried out under a local anaesthetic, it is a notable fact that some examples are so extremely painful and tender that the local anaesthetic is ineffective; a general anaesthetic is then usually necessary. X-Ray therapy is not satisfactory.

SECTION ELEVEN.

A COMPARISON OF CONGENITAL AND TRAUMATIC ARTERIO-VENOUS FISTULAE.

DIFFICULTIES IN DIAGNOSIS.

In certain instances, admittedly few, it may be difficult or impossible to arrive at an adequate decision. During birth, the infant's skull may be so damaged that, should a cirsoid aneurysm of the scalp develop soon afterwards, it may well be classified in either category. Another source of error is that a congenital lesion may lie dormant for many years in the form of a haemangioma and then, either for no apparent reason or more often after an injury, it may begin to enlarge and produce all the effects of arterio-venous fistulae. An illustration is also provided by a case, reported first by Yater as traumatic and later by Horton & Ghormley (95) as congenital, in whom an injury at the age of twenty produced an aggravation of a congenital abnormality in which there was hypertrophy of a limb of long standing. On the other hand, a traumatic cirsoid aneurysm may wrongly be suspected to be congenital, when it develops after so mild an injury that little attention was paid to it at the time.

The history, however, is usually definite enough, and in congenital cases some obvious lesion has been noted since birth. In traumatic cases, there is evidence either of a wound due, for example, to a stab or a bullet, or of a blunt blow, as in a cirsoid aneurysm. The traumatic type is much more common than the congenital.

IMPORTANT RESEMBLANCES AND DIFFERENCES.

Taking, for ease of comparison, a typical congenital lesion in the lower limb, such as found in Case Four, and a traumatic lesion of the femoral vessels, it will be noted how certain local and general features are similar and others different. From the structural standpoint, with very few exceptions, in a traumatic case the fistula is single and large, while in a congenital case there are multiple small fistulae present over a considerable length of the main vessels and perhaps their branches also. The traumatic type may take the form of a varicose aneurysm, with a false sac present in relation to the wound in the artery, or of an aneurysmal varix, with a direct communication, but the /

the essential effects are the same and are due to the actual fistulous track, except that the latter type may close spontaneously; there is no aneurysmal sac in the congenital case. Proximal dilatation and distal contraction of the main artery, proximal and distal dilatation of the main vein, abnormal pulsation, a thrill and a bruit are all signs which are more constant and more pronounced in traumatic cases.

The congenital lesion very frequently takes the form of the syndrome of hypertrophy of the affected part, haemangiomata and varicose veins. In the traumatic lesion, hypertrophy may develop if the fistula has been present for several years during the period of growth, but it is most unlikely to attain the degree of gigantism found in the congenital type; varicosities are certainly a feature but haemangiomata are absent, although a reddish blush may be present in the vicinity of the fistula. In both types there may be a brown pigmentation of the skin distal to the fistula.

The effects on the circulation in the distal part of the limb are of great importance and are demonstrable in various ways. In the congenital case, the affected limb has a uniformly higher temperature than the opposite limb and has adequate distal arterial pulsations, whereas in the traumatic case there is an increase in temperature in the vicinity of the fistula with a decrease in the peripheral temperature and poor distal pulsations. At any time, in both types, signs of failure of the circulation may develop, such as cyanosis, oedema, ulceration or gangrene. In the traumatic case, provided the immediate effects of the arterial injury are overcome, there may be no outstanding danger to the peripheral circulation, and in fact after three to six months the fistula becomes a stimulus to an adequate collateral circulation. Temporary occlusion of the traumatic fistula by digital pressure may actually restore to normal an absent or deficient distal pulse, and Matas recommended such daily compression as a necessary preliminary to operative cure of the fistula. In the congenital case, each of the multiple fistulae may act as a stimulus to the collateral circulation and the distal part of the limb has a good supply of blood. In spite of that, however, local circulatory disturbances tend to be progressive and gangrene is common.

The general cardio-vascular effects also differ. In the traumatic type, there usually develops a congestive cardiac failure of a progressive nature, with dilatation of the heart, pulmonary oedema, liver enlargement, ascites and oedema of the limbs; the larger the fistula, the more rapid and severe are these changes. Such evil manifestations are rare in the congenital /

congenital case and tend to be gradual in their development, reasons being the smaller size of the fistulae and the better adaptability of the cardiovascular mechanism when the abnormality exists from birth. The Branham-Nicoladoni bradycardia reaction is found in both types, but chiefly in the traumatic. In both types, also, these cardiovascular effects may disappear completely after a successful operation or after amputation.

Operative cure of arterio-venous fistulae is often difficult in either type on account of the technical difficulties such as inaccessibility of the fistula and intense vascularity around it. In the usual traumatic type, only one fistula has to be dealt with, and an excellent result will follow, provided a suitable operation is chosen to obliterate the fistula and as long as the distal circulation is maintained. In the congenital type, although several fistulae may be closed satisfactorily, there is a great risk of some being overlooked or of others unexpectedly becoming patent at a different level and at a later date. In spite of several recorded successful results after closure of multiple fistulae, it is unfortunate that amputation frequently becomes necessary.

Matas (208) and Makins (209) are amongst the greatest authorities on traumatic arterio-venous fistulae, and excellent accounts on both traumatic and congenital types have been given by Pemberton and Saint (35), Reid (72, 73, 74, 75) and Holman (61).

SECTION TWELVE.

REVIEW OF TREATMENT.

THE AIM OF TREATMENT.

In congenital vascular anomalies, complex changes are present and treatment may have to be designed for more than one purpose, for example, the removal of a disfiguring haemangioma of the face, the closure of arterio-venous fistulae causing embarrassing local or general circulatory effects, or the equalisation of asymmetrical limbs. Accordingly, no single method can be asserted as the best, and any method must be adjusted to the pertinent circumstances. The two important subjects of the treatment of the vascular lesions and of the skeletal abnormalities will now be reviewed independently.

THE VASCULAR LESIONS.

Haemangioma.

It is possible for spontaneous cure to occur, particularly during the first year of life, but if it does not happen then, there is a tendency for enlargement to take place in subsequent years. Except for a disfiguring lesion of the face, many superficial capillary haemangiomata may be better left alone and may never give rise to any disability. Different methods of treatment have been advocated for the various types of haemangioma, but it is not proposed to do more than mention the views of a few selected authors, including Shaw (176), Bailey, W. and Kiskadden (210), Berson (214), and Pohle and McAneny (213).

The local application of caustics, especially carbon dioxide snow, proves quite effective for small, localised, capillary lesions. For the flat capillary type or port wine stain of larger size, excision of the lesion and full thickness skin grafting are very satisfactory. In such a case, X-Ray treatment is unsatisfactory as it does not improve the condition and may produce a telangiectasia more unsightly than the original lesion.

For the cavernous haemangioma, radium treatment is particularly good in children when the lesion is sensitive and it can be applied in the form of an implant to give a dosage of 2000r. For certain types, deep X-Ray treatment with a dosage of 400r at two monthly intervals gives a satisfactory result, with little skin atrophy and no epilation. Unless applied with /

with the greatest of skill, however, any form of radiotherapy may produce telangiectasia, pigmentation, excessive blanching, dense sclerosis or atrophy of the skin. Contact roentgen irradiation with the Chaoul tube is recommended by Kerr, H.D. (216) but this method and also the use of carbon dioxide snow and the β rays of radium, are generally believed to be bad and dangerous in deep seated haemangiomata. Another important danger of any method of radiotherapy in children is the liability to disturbance of the growth of bone by damaging the epiphyseal cartilages; Kaplan (212) claimed, however, that the danger was avoidable with good technique.

In view of the above difficulties, surgical excision of a cavernous haemangioma may be preferable, provided the site is accessible and the size not too great. The operation should consist of excision of the main mass of vessels and the ligation of entering vessels, and it may be combined with the use of an endothermic current for excision or coagulation. The injection of sclerosing solutions, such as lithium salicylate, quinine urethane or sodium morrhuate, has recently proved effective in cavernous lesions, and several authors, such as Light (211), have strongly recommended it; the injections may be used alone or in conjunction with operation. The radioopaque solutions used in diagnosis have also been shown to have a satisfactory sclerosing action.

Electrolysis is a method which was strongly supported by Duncan (10) for the treatment of all classes of haemangioma, including those which seemed to be cirsoid aneurysms, and in his hands it proved very effective. Shaw (176), among others, strongly criticised the method as being uncertain in its results and actually dangerous on account of the severe oedema which might follow, especially when applied in the region of the mouth and neck.

Phlebectasis.

In many cases of this nature, the appearances of the veins are simply those of the ordinary type of varicose veins and the same method of treatment is quite efficient. The most satisfactory method has been the ligation and division of the enlarged venous trunk at two or more levels, local anaesthesia being used. If a venogram is being taken simultaneously, the radioopaque solution is found to encourage thrombosis, or if this investigation is not made, the vein should be injected at the time of operation with a sclerosing agent. The wearing of elastoplast bandages to the whole limb is recommended for two to three weeks after operation. Healing of the wounds tends to be slow and there may be a continued oozing of blood /

blood from the wounds for several weeks after operation. In some cases which are quite typical of phlebectasis, a small arterial communication may exist, and it may then be necessary to ligate it as well as carrying out the above method.

In the most severe cases, there is a very widespread development of enlarged veins, not confined to the distribution of a single trunk, and it may not be possible to apply adequate treatment. Ligation of such veins is unlikely to be effective but the injection of sclerosing solutions is simple and often quite satisfactory. Any form of radiotherapy tends to be worthless, as the vessels are well formed with normal endothelium, and no more radiosensitive than any other normal blood vessels.

Arterio-Venous Fistulae.

Such lesions are notoriously difficult to treat on account of the multiplicity of the fistulae, the difficult operative approach through vascular tissues, the possible inaccessible site and the tendency for new fistulae to become apparent after operation. Horton, quoted by Franklin (124), stated that the condition is always made worse by attempts to isolate or close the fistulae, and, apart from the orthopaedic correction of unequal limbs, he merely recommended amputation of the affected limb in severe cases with systemic effects. Several operations are possible, however, and may meet with success.

Proximal arterial ligation consists in the ligation of a main artery at a level proximal to the fistulae, without any interference with the actual fistulae or the corresponding vein. Originally applied to traumatic cases, it has also been used in congenital cases, but, though condemned for over a century, it is still occasionally practised with effects almost invariably bad. Thus it is very frequently followed by gangrene of a limb when no sign of gangrene existed previously, and, on the other hand, it may result in a progressive increase in activity of the lesion, after a short lived improvement. In some circumstances, it may be the only possible alternative to amputation of a limb and it may then be justifiable. The only other indication is a carotid-cavernous sinus fistula, where the site is inaccessible and a ligation of the common or internal carotid artery in the neck is performed.

The ideal operation is performed when each fistulous communication can be dissected out individually and then ligated and divided, without the necessity of ligating any main artery; the case of Rienhoff (22) was an excellent example of the success of this method. A similar type of operation may also be employed with excision /

excision of masses of veins or the injection of sclerosing solutions into remaining veins. Akin to that so successful in traumatic cases, the operation of quadruple ligation may give good results; it consists in the ligation of the main artery and the main vein both proximal and distal to the fistulae. The injection of sclerosing solutions into masses of dilated veins has also been recommended by Smith, F.L. and Horton (96) as the sole method of treatment and it may prove quite satisfactory.

The danger after many of the operations is interference with the blood supply beyond, producing gangrene of a limb or cerebral anaemia in the case of operations on the common or internal carotid arteries. Thus it happens that amputation of a limb may be the final step in treatment after previous attempts at conservative surgery. In addition, amputation may be necessary as the original operative treatment in rapidly progressive cases, especially those associated with cardiac failure, and amputation of a digit is advisable in a lesion localised to that site. In order to make operations on the fistulae more complete and safer, and to avoid the risk of post operative gangrene, Mason (172) suggested the preoperative use of the negative and positive pressure apparatus of Hermann, and claimed improved results.

Cirsoid Aneurysm.

Under this heading, the treatment of the typical cirsoid aneurysm of the scalp will be reviewed, references to both congenital and traumatic types being included owing to their close similarity. The so called cirsoid aneurysm of a limb is better considered under the heading of arterio-venous fistulae.

Among the older methods of treatment is the transfixion of the vascular swelling by several skewers or needles, the protruding ends of which are then held approximated by elastic pressure; this alone may induce thrombosis of the vessels by a process of strangulation and an adjunct may be the passage of an electric current through the needles, as described by Beaumont (9). Interlocking scalp sutures may act in a similar manner. Direct pressure over the cirsoid aneurysm and the application of caustics to the surface are unreliable methods and may induce attenuation of the skin, ulceration or haemorrhage.

Reid (75) in a full review of the subject, advised that a cirsoid aneurysm should be dealt with early and completely before arterio-venous anastomoses have produced such formidable changes that operation becomes dangerous or impossible. Before commencing treatment /

treatment it may be advisable to carry out arteriography in order to define the limits of the lesion accurately. Of the several operative methods described, proximal ligation of one or more entering arteries is seldom if ever effective as an isolated procedure. There may be a temporary improvement but sooner or later collateral channels form and the condition then becomes more difficult than ever to treat. As a preliminary to other measures, however, it is definitely advantageous as it reduces the vascularity of the affected part to less dangerous limits at the time of the next step.

As a second stage, a horse shoe shaped incision is popular, the flap consisting of the whole thickness of the scalp; all divided vessels are ligated and the mass of vessels is dissected off the deep surface of the flap, as described by Rundle (66). Kerr, R.A. (45) at the same time used a rubber tube around the head as a tourniquet. Searby (215) devised a rather different operative procedure, and at the first stage a flap incision was made, all vessels in the wound were ligated, and the flap was replaced over a pack, firm pressure being maintained thereafter for seventy two hours. At the second stage, the vessels in the flap were found to be thrombosed and were easily dissected away, the pedicle being ligated. Roche (38) carried out the rather unusual step of excising a disc of the complete thickness of the scalp, in addition to the ligation and excision of vessels.

A much simpler method, and an effective one, is that recommended by Patey (178), in which proximal ligation of the external carotid is followed merely by the injection of a sclerosing solution into one of the large veins forming the swelling.

Radiotherapy is seldom advisable, but Eckhoff (91) used radium as an adjunct to operative measures in a particularly difficult resistant lesion on the chest wall.

THE SKELETAL DEFORMITY.

Surgical Methods.

Asymmetry in the upper limbs calls for no treatment, but, in the lower limbs, it may be the cause of such considerable disability that some method of correction is demanded, although, as Phemister pointed out, there is occasionally a tendency to equalisation of the limbs later. The shorter limb is almost always the normal, and a very simple measure is to fit this limb with a high boot to compensate for the difference in length /

length. This generally proves quite satisfactory in children and may be continued in adult life.

Although operations on the bones during the period of growth are considered by many to be undesirable, Phemister (146) has devised the ingenious operation of epiphyseo-diaphyseal fusion about the knee, and he advocated the method as safe and satisfactory, provided care is exercised in the choice of time and location, and the number of epiphyses to be fused. The operation aims at retarding growth in the longer limb so as to equalise the length of the two limbs by the time adult life has been reached. Incisions are made on the medial and lateral sides of the knee to expose the lower end of the femur and the upper ends of the tibia and fibula. At each site, a piece of cortex, 3 X 1½ cms. is excised, crossing the cartilage line and including about 1 cm. of epiphysis. The sides of the cartilaginous disc, anterior and posterior to this, are chiselled out to a depth of approximately 1 cm. and the transplant is reinserted with the ends reversed.

If growth has ceased before attempts have been made to equalise the limbs, it is possible to aim at shortening the longer limb by resection of a portion of the shaft of the femur or of the tibia and fibula. As an alternative, lengthening of the shorter limb has been favoured by Abbott (217), the results being good in his hands, but the operation is difficult and has the disadvantage of interfering with the normal limb.

The operation of sympathectomy has been suggested as an indirect method of stimulating growth in the shorter limb, but the results are conflicting, as discussed in Section Eight. Harris, R.I. and McDonald (128) declared that a prolonged increase in blood supply, produced by lumbar sympathectomy, can result in an acceleration of the rate of growth. On the other hand, Harris, K.E. and Wright, G.P.(32) decided that the operation was of no benefit, it being suggested that the nutrient arteries to bones and epiphyses were encased in such a rigid structure that they could not dilate. McMaster and Roome (130) noted that the arterial hyperemia produced by a lumbar sympathectomy could not be expected to have a stimulating effect on bone growth.

McMaster and Roome, and also Pearse and Morton (145), believed that venous stasis hastens growth, and consequently a method of producing continued passive congestion, as by venous ligation, might be expected to increase the size of the shorter limb. Tavernier (85) suggested the method of producing venous stasis with an Esmarck's rubber bandage applied round the limb, and he also approved of irritation of a bone for the same purpose.

Wu/

Wu and Miltner (131), in animal experiments, were able to stimulate growth in length by the procedure of loosening or stripping the periosteum of the shaft of a bone, although no satisfactory account of the clinical application of the method is available.

Surgical methods may be required for the correction of secondary skeletal deformities produced by the inequality of the limbs. A notable illustration was the case reported by Thomson (43), where severe chronic sacro-iliac arthritis was caused by the disturbed mechanics of the joints, so that ultimately bilateral fusion of the sacro-iliac joints became necessary.

Radiotherapy.

The dangerous effects of X-Ray and radium treatment on the growth of bone have already been discussed in Section Eight, but, if applied carefully and deliberately, one of these agents may be of great value in the correction of asymmetry of the limbs. The aim of the treatment is to irradiate one or more epiphyseal cartilages in the longer limb, so that growth is interfered with to such an extent that ultimately the limbs become of the same length by the time adult life is reached. A moderate dosage produces retardation and a larger dosage complete cessation of growth at the site irradiated, and it is, therefore, essential to regulate the dosage so that eventual stunting of what was the longer limb is not induced. Desaive (143) applied a collar of columbia wax containing radium at the level of three epiphyses, the lower femoral and the upper and lower tibial; four years later, the difference in size of the two limbs was much less, as the treated limb had failed to grow as much as the normal. Deep X-Ray treatment, however, is equally as satisfactory as radium.

An angioma of bone is another indication for radiotherapy, which has been recommended by such authorities as Anspach (138), and Geschickter and Maseritz (139). Occasionally, as in Case Three, radiotherapy may be employed for the double purpose of treating the angioma and of interfering with growth at the adjacent epiphyseal cartilage.

Plastic Procedures.

Plastic operations designed to reduce the girth of a hypertrophied limb are seldom if ever applicable to blood vascular anomalies, although the Kondoleon type of operation was applied by Shumacker (112) to a case with an associated abnormality of the lymphatics. A plastic operation of a similar nature is contemplated in Case Twelve, in order to reduce the size of the cartilage of the auricle.

SECTION THIRTEEN.

SUMMARY.

A series of twelve cases of rare congenital vascular anomalies was studied in detail, with the most modern methods of investigation. An extensive review of the literature revealed more than three hundred and fifty examples of a similar nature but it was not possible to state any accurate figure on account of the uncertainty of some descriptions and the confused nomenclature used in the past. The abnormalities were usually obvious at or soon after birth, but occasionally they did not attract attention for several years. A wide range of clinical and pathological features was noted, and the most important and constant of these were discussed.

Interest in the subject was first aroused in the triad of localised hypertrophy, varicose veins and haemangiomata, which was found to have been described in the past as a purely separate entity and also as among the phenomena of arterio-venous fistulae. There appeared to be no justifiable distinction between these types, and it was shown, as a result of special tests, that arterio-venous fistulae might exist in the absence of the typical signs of abnormal pulsations, a thrill and a bruit. The fistulae, occurring in different situations, could exhibit many peculiar manifestations and were not necessarily associated with hypertrophy. Thus the investigation was directed towards cases showing the above triad, with or without arterio-venous fistulae and conveniently classified as haemangiectatic hypertrophy, and also towards cases showing evidence of arterio-venous fistulae, irrespective of other findings.

In the personal series, Cases Three, Four and Eleven showed the most classical appearance of hypertrophy of a whole limb, haemangiomata and varicose veins, the diagnosis of arterio-venous fistulae being beyond doubt. Cases One and Ten demonstrated the same triad, but in an irregular manner and in more than one limb, and without proof of arterio-venous fistulae. In Cases Five and Twelve, there were well localised pulsatile lesions, due to arterio-venous fistulae and of the type known as a cirsoid aneurysm. Cases Two, Six, Seven and Eight were of the type of so-called cavernous haemangioma, characterised by an extensive development of veins and numerous phleboliths, and, except in Case Two, arterio-venous fistulae were shown to exist. Case Nine was an example of painless glomangiomata, one lesion being large and showing the signs of arterio-venous fistulae.

A /

A plea was advanced for a more simplified classification of these complex anomalies. Although diverse in their manifestations, they should be studied as a whole, and attempts to divide them into separate independent classes are to be deprecated. Except for the glomangioma, it should be possible to trace their origin to errors in the development of the blood vascular system, probably at about the fourth week. The abnormality may arise in angioblastic cells, or in the developing vessels at the capillary net stage, the retiform stage or the stem stage. Congenital arterio-venous fistulae can be traced at the retiform stage to a failure of separation of the arterial and venous trunks from the original capillary plexus. Phlebectasia can be accounted for at the same stage by the persistence of excessive communications between veins and capillaries, and so also cavernous haemangiomata, which may be indistinguishable from it. Most capillary haemangiomata are due to errors in the capillary net stage. An error at the stem stage is unusual and gives rise to a vessel of anomalous structure in an abnormal site.

Congenital arterio-venous fistulae are very rarely single and are generally multiple, but in certain cases some may remain latent for years, becoming obvious after an injury or being recognised only after the elimination of other fistulae. The fistulous track may be short and direct between large vessels, or it may start as a definite small artery and merge imperceptibly with a venous plexus. There are usually dilatation and thinning of the main artery proximal to the fistulae, and contraction of it beyond, whereas the veins undergo an increased development, dilatation and thickening of the wall, both proximal and distal to the fistulae. The flow of blood passing directly from the artery into the veins may give rise to pulsation in the veins, a palpable thrill and an audible bruit. The parts distal to the fistulae may suffer from a decreased blood supply as a result of this short-circuiting, but nevertheless may appear quite vascular on account of venous congestion. In an advanced case, the circulation becomes so deficient that changes supervene such as ulceration, haemorrhage, and gangrene, amputation then being demanded. Special tests, particularly the estimation of the oxygen content of the venous blood and less so arteriography, are of paramount importance in determining the presence and the site of the fistulae. A comparison was drawn between congenital and traumatic arterio-venous fistulae.

Varicosities of the veins are a prominent feature, both in the presence and in the absence of arterio-venous fistulae, but from the clinical examination alone it is not necessarily possible to make a decision /

decision. They may have the appearances of the common type of varicose vein of the lower limb, confined chiefly to the long saphenous vein or occasionally to an abnormally situated one entering the buttock. Enlarged veins form almost the whole of the mass of vessels in a cirsoid aneurysm and in cavernous haemangiomata, and they also may have an intimate connection with overlying capillary haemangiomata. Phlebitis is an occasional complication and phleboliths assume great prominence if the flow of blood in the veins is sluggish; any other complication of varicose veins may also occur.

Although the object of the investigation did not concern haemangiomata in general, it was found necessary to review the subject widely. Many varied views were quoted, the chief controversy being whether a vascular maldevelopment or a vascular tumour was the essential pathology and the term hamartoma being suggested as a compromise. Judging from my own studies, it appears that a developmental anomaly is the cause of haemangiomata in the type of case being investigated, if not in many others. The behaviour of these lesions and their multiplicity in no way suggest a tumour growth, and there is a very close association with the other abnormalities. A view expressed in the past is that there is an intimate connection between the boundaries of a haemangioma and the distribution of the nerve supply to that part, but no personal support can be given to it, the vascular influences being predominant. It is generally agreed that there do exist true vascular tumours, both simple and malignant, such as haemangioma simplex, compact haemangioma, haemangio-endothelioma and Kaposi's haemorrhagic sarcoma. There were also discussed several aspects of multiple lesions, such as those bordering on malignancy, and the rare occurrence of a tumour in an obvious anomaly. Several other conditions and syndromes resembling or associated with haemangiomata were mentioned, for example, telangiectases, Sturge-Weber syndrome, Maffucci's syndrome.

The subject of glomangioma was reviewed. Though the lesion is typically small, single, painful and situated in the digits, it is now appreciated that other features occur. The personal case reported was unusual, as the lesions were multiple and painless, one being large and perhaps the first recorded example of a glomangioma to show the signs of arterio-venous fistulae. It is surprising, however, that this complication does not occur more often, considering that a glomangioma is derived from the normal arterio-venous anastomosis. The views on the pathology are not uniform, once again a tumour growth and an aberration in development having to be contested.

General cardio-vascular phenomena are common,

though /

though seldom of the severity found in traumatic arterio-venous fistulae. In carrying out one test, especially in phlebectasia, the patient assumes the erect posture from recumbency, whereupon so much blood passes into stagnant veins and large haemangiomata of the lower limb that the effects of a haemorrhage are reproduced, consisting of a sudden increase in the pulse rate, a lowering of the systolic and a raising of the diastolic blood pressure. In arterio-venous fistulae and cirsoid aneurysms, the interesting Nicoladoni-Branham brady-cardia reaction is demonstrated by pressure to occlude the fistula, the sudden raising of the systolic blood pressure and the slowing of the pulse rate being evidence of an immediate vagal response. These two tests, though apparently opposite, are really similar, the former being due to the escape of blood from the active circulation, and the latter to its escape being prevented. Fatigue is one of the earliest symptoms of cardiac disability. Only rarely in congenital arterio-venous fistulae does a severe degree of congestive cardiac failure develop, which, however, rapidly re-covers if the fistulae are eliminated or if an affected limb is amputated. Special tests, such as the estima-tion of the blood volume, are of doubtful significance in congenital cases.

The hypertrophy of bone and auricular cartil-age was discussed in detail, and there were reviewed important, seldom mentioned facts on the effects of vascular influences on their growth. The most commonly expressed theory is that arterio-venous fistulae cause an increased flow of blood in the arteries, thereby allowing extra nutrition to the parts supplied, but in my opinion it has so many weaknesses that it should be rejected. Venous stasis, on the other hand, is eminent-ly more acceptable and is applicable to both bone and cartilage. The hypertrophy, which may affect all the structures in the affected part, is not necessarily due to any vascular influences, however, and it is possible that the hypertrophy and the vascular lesions are con-comitant features, arising independently from a common error in the development of mesoderm. Several patho-logical changes are also to be noted in the bones, especially on X-Ray examination, and they include an overgrowth of vascular channels, arterio-venous fistulae, and haemangioma. Severe stunting is a sequel of in-tensive X-Ray or radium treatment, irreparable damage being inflicted on the epiphyseal cartilages.

The prognosis is variable. In cases of phlebectasia and arterio-venous fistulae of minor de-gree, it is quite good and similar to that of ordinary varicose veins, except for the inconvenience of en-largements of the limb or digits. In those of the cirsoid aneurysm type, the prognosis is bad if untreated and /

and is good only if the fistulae can be eliminated by treatment. In arterio-venous fistulae with a giant limb, it is only rarely possible to close all fistulae; otherwise it is better to avoid operation on the vessels and to secure adequate orthopaedic correction. Amputation of a limb has always to be considered in prognosis, but it is chiefly required for gangrene or severe progressive cardiac effects. The prognosis is generally bad if bone and muscle are extensively traversed by large vessels, and it may be serious in the region of the mouth and throat. The glomangioma carries a good prognosis as it can be easily excised.

A full discussion was made on the many recommended methods of treatment. It tends to be unsatisfactory in the presence of multiple fistulae, but conspicuous success may follow boldly planned operations at an early stage. In addition to the surgical care of both the vascular and the skeletal lesions, the therapeutic and destructive effects of irradiation were demonstrated.

SECTION FOURTEEN.

REFERENCES.

1. BUSHE, G. Excision of an Anastomosing Aneurysm. Lancet, 1827-8, 2, 413.

2. ADAMS, J. Singular Case of Hypertrophy of Right Lower Extremity, with Superficial Cutaneous Naevus of Same Side. Lancet, 1858, 2, 140.

3. PEMBERTON, O. Aneurysm by Anastomosis. Lancet, 1860, 1, 516.

4. HEWETT, P. Case of Congenital Aneurismal Varix. Lancet, 1867, 1, 146.

5. LEE, H. Case of Aneurismal Varix. Lancet, 1867, 1, 147.

6. SMITH, SIR T. Angiectasis of Hand and Fingers. Trans. Clin. Soc. London, 1882, 15, 198.

7. FINLAYSON, J. Congenital Unilateral Hypertrophy and Patches of Cutaneous Congestion. Glasgow Med. J., 1884, 22, 327.

8. LITTLE, J.F. A Case of Naevus involving whole of Right Side. Trans. Clin. Soc. London, 1893, 26, 243.

9. BEAUMONT, W.M. Cirsoid Aneurysm of Orbit, Forehead and Scalp. Brit. Med. J., 1897, 2, 273.

10. DUNCAN, J. Angioma and Other Papers, 1900, 1-39. Edinburgh: Oliver and Boyd.

11. KLIPPEL, M. and TRENAUNAY, P. Du Naevus Variqueux Osteohypertrophique, Arch. Gén. de Méd., 1900, 185, 641.

12. BERRY, J. Large Arterio-Venous Aneurysm of Neck. Lancet, 1906, 2, 1714.

13a. DAVIS, J.S. Primary Haemangiomata of Muscle. Johns Hopkins Hosp. Bull., 1908, 19, 74.

13b. DAVIS, J.S. and KITLOWSKI, E.A. Primary Intramuscular Haemangioma of Striated Muscle. Arch. Surg., 1930, 20, 39.

14. DENT, C.T. "Congenital Elephantiasis" of Arm. Proc. Royal Soc. Med.; Sec. Study Dis. Child., 1911, 4, 24.

15 /

15. HALSTED, W.S. Congenital Arteriovenous and Lymphaticovenous Fistulae. Trans. Amer. Surg. Ass., 1919, 37, 262.

16. TELFORD, E.D. Hemihypertrophy of Body with Naevus and Varicose Veins. Lancet, 1912, 2, 1291.

17. BLAND-SUTTON, SIR J. Spolia Opima - Section on a Rare Angioma. Brit. Med. J., 1918, 2., 593.

18. ARMOUR, D. Case of Cirsoid Aneurysm of Hand. Trans. Med. Soc. London, 1919, 42, 237.

19. WAKELEY, C.P.G. Calcification of Angiomata. Arch. Radiol. and Electrother., 1920-1, 25, 363.

20. MELENEY, F.L. Pathological Study of a Case of Cirsoid Aneurysm. Surg., Gynec. Obstet., 1923, 36, 547.

21. ELKIN, D.C. Cirsoid Aneurysm of Scalp. Ann. Surg., 1924, 80, 332.

22. RIENHOFF, W.F. Congenital Arterio-Venous Fistula. Johns Hopkins Hosp. Bull., 1924, 35, 271.

23. McFARLAND, J. Surgical Pathology, 1924, 258. London: Lewis.

24. STEWART, S.F. and BETTIN, M.E. Motor Significance of Haemangioma. Surg., Gynec. Obstet., 1924, 39, 307.

25. BERNHEIM, B.M. Congenital Arterio-Venous Fistula of Left Brachial Artery and Vein. Ann. Surg., 1925, 81, 465.

26. PATERSON, D. and WYLIE, W.G. Hypertrophy of Bones of a Limb due to a Naevus. Brit. J. Child. Dis., 1925, 22, 36.

27. BELL, G. and INGLIS, K. Haemangioma of Leg. Brit. J. Surg., 1925-6, 13, 696.

28. BEATTY, C.C. Haemangiectatic Hypertrophy of Arm. Proc. Roy. Soc. Med., 1926-7, 20, 532.

29. HARBIN, M. Overgrowth of Long Bones of Lower Extremity. Arch. Surg., 1927, 14, 142.

30. SUSMAN, E. and McCREDIE, D.W. Haemangiectatic Hypertrophy of Arm. Med. J. Austral., 1927, 2, 581.

31. GRAY, A.M.H. Haemangiectatic Hypertrophy. Proc. Roy. Soc. Med., 1927-8, Vol. 21, part 2, p.1431.

32 /

32. HARRIS, K.E. and WRIGHT, G.P. Case of Haemangiectatic Hypertrophy of a Limb. Heart, 1929-31, 15, 141.

33. PAUTRIER, L.M. and ULLMO, A. Hémangiectasie Hypertrophique de Parkes Weber. Bull. Soc. Franc. de Dermat. & Syph., 1928, 35, 981.

34. LYLE, H.H.M. Haemangioma of Chest Wall. Ann. Surg., 1928, 88, 668.

35. PEMBERTON, J. de J. and SAINT, J.H. Congenital Arterio-Venous Communications. Surg., Gynec. Obstet., 1928, 46, 470.

36a. MATAS, R. Congenital Arterio-Venous Angioma of Arm. Ann. Surg., 1940, 111, 1021.

36b. MATAS, R. and HENINGER, B.R. Reversible Cardiac Enlargement in a Case of Congenital Cavernous Haemangioma. Amer. Heart J., 1939, 17, 131.

37. PATEL, M. Anéurisme Cirsōide du Cuir Chevelu. Lyon Chir., 1929, 26, 414.

38. ROCHE, A.E. Excision of Arterial Angioma. Clin. J., 1929, 58, 269.

39. WILBUR, D.L. Multiple Aneurysms of Arteries of Right Arm, associated with Arterio-Venous Fistula and Arterial Embolism. Amer. J. Med. Science, 1930, 180, 221.

40. SCHLOFFER, H. Changes in a Racemose Arterial Angioma. Deutsche. Ztschr. f. Chir., 1930, 225, 339. Abstract in Inter. Abst. Surg., (Surg., Gynec., Obstet.) 1931, 52, 272.

41. LEWIS, D. de W. Congenital Arterio-Venous Fistulae. Lancet, 1930, 2, 621 and 680.

42. SORREL, E. Angiome Diffus du Membre Inférieur Droit. Bull. et Mém. Soc. Nat. Chir., 1932, 58, 758.

43. THOMSON, J.E.M. Haemangiectatic Hypertrophy and Sacro-Iliac Disturbance. J. Bone and Joint Surg., 1932, 14, 702.

44. BLUMGART, H.L. and ERNSTENE, A.C. Haemangiectatic Hypertrophy and Congenital Phlebarteriectasis. Arch. Int. Med., 1932, 49, 599.

45. KERR, R.A. Plexiform (Cirsoid) Aneurysm of Scalp. Brit. Med. J., 1933, 2, 566.

46a. WAKEFIELD, E.G. Hypertrophy, Congenital, of Left Shoulder Girdle, Arm and Hand, with Naevus and Varicose Veins. Amer. J. Med. Science, 1926, 171, 569.

46b/.

46b. WAKEFIELD, E.G. and HINES, E.A. Congenital Hemihypertrophy. Amer. J. Med. Science, 1933, 185, 493.

47. LASKEY, N.F. Circoid Aneurysm. Amer. J. Surg., 1933, 20, 128.

48. BRODERICK, R.A. and ROUND, H. Cavernous Angioma of Maxilla. Lancet, 1933, 2, 13.

49. SMITH, A.G. Cirsoid Aneurysm of Scalp. Brit. Med. J., 1934, 1, 147.

50. GOUGEROT, H. and LORTAT-JACOB, E. Naevus Variqueux Ostéohypertrophique. Bull. Soc. Franc. de Dermat. et Syph., 1934, 41, 1668.

51. DE TAKATS, G. Vascular Anomalies of Extremities. Surg., Gynec., Obstet., 1932, 55, 227.

52. DE TAKATS, G. and MACKENZIE, W.D. Diagnosis and Treatment of Circulatory Disturbances of Extremities. Surg., Gynec., Obstet., 1934, 58, 655.

53. COUCH, J.H. Haemangioma with Fracture through Invaded Bone. Canad. Med. Ass. J., 1935, 33, 416.

54. ALAJOUANINE, T., THUREL, R., et HORNET, T. Un Cas d'Anéurysme Cirsoïde de la Main avec Osteoporose. Rev. Neurol. 1935, 63, 724.

55. DAVID, V.C. Aneurysms of Hand. Arch. Surg., 1936, 33, 267.

56. FREUND, E. Diffuse Genuine Phlebectasia. Arch. Surg., 1936, 33, 113.

57. VEAL, J.R. and McCORD, W.N. Congenital Abnormal Arteriovenous Anastomoses of Extremities. Arch. Surg., 1936, 33, 848.

58. PEABODY, C.W. Hemihypertrophy and Hemiatrophy. J. Bone and Joint Surg., 1936, 18, 466.

59. KIDNER, F.C. Diffuse Cavernous Angioma of Leg. Surg., Gynec., Obstet., 1936, 63, 647.

60. GILMOUR, J. and BOLAM, M. Congenital Arterio-Venous Communications. Brit. J. Surg., 1937-8, 25, 337.

61. HOLMAN, E. Arterio Venous Aneurysm, 1937, 93. New York: MacMillan.

62. CHANDLER, F.A. Local Overgrowth. J. Amer. Med. Ass., 1937, 109, 1411.

63 /

63. BELUFFI, E.L. Cirsoid Aneurysm. Policlin, Rome, 1937, 44, sez. chir. 221. Abstract in Inter. Abst. Surg., (Surg., Gynec., Obstet.) 1937, 65, 448.

64. ROSENAK, S. Spontaneous Arterio Venous Connections. Wiener klin. Woch., 1937, 1, 962. Abstract on Inter. Abst. Surg., (Surg., Gynec., Obstet.) 1938, 67, 378.

65. PAUTRIER, L.M. et LANG, A. Hémangiectasie Hypertrophique. Bull. Soc. Franc. de Dermat. et Syph., 1937, 44, 605.

66. RUNDLE, F. Case of Cirsoid Aneurysm of Scalp. Brit. J. Surg., 1937-8, 25, 872.

67. TOURAINE, A., DUPERRAT, R. et BAUDOUIN, A. Angiome Radiculaire, Caverneux et Verruqueux. Bull. Soc. Franc. de Dermat. et Syph., 1938, 45, 577.

68. PEYTON, W.T. and LEVEN, N.L. Haemangioma and its Treatment. Surgery, 1938, 3, 702.

69. WISE, W.D. and LISANSKY, E.T. Congenital Arterio Venous Fistula. Ann. Surg., 1938, 108, 701.

70. WRIGHT, A. DICKSON. Congenital Arterio Venous Aneurysm of Thigh. Trans. Med. Soc. London, 1938, 61, 62.

71. WARD, G.E. and JONAS, A.F. Metastasising Haemangioma simulating an Aneurysm. Arch. Surg., 1938, 36, 330.

72. REID, M.R. Studies on Abnormal Arterio Venous Communications, Acquired and Congenital. Arch. Surg., 1925, 10, 601.

73. REID, M.R. Ibid. 1925, 10, 996.

74. REID, M.R. Ibid. 1925, 11, 25.

75. REID, M.R. Ibid. 1925, 11, 237.

76. REID, M.R. Report on Vascular Lesions. Amer. J. Surg., 1931, 14, 17.

77. REID, M.R. and McGUIRE, J. Arterio Venous Aneurysm. Ann. Surg., 1938, 108, 643.

78. SEEGER, S.J. Congenital Arterio Venous Anastomoses, Surgery, 1938, 3, 264.

79 /

79. O'NEIL, E.E. Congenital Arterio Venous Fistula. New Engl. J. Med., 1939, 221, 133.

80. NEWSON, A.L. Case of Sturge's Disease. Brit. Med. J., 1939, 2, 1088.

81. PACK, G.T. Tumours of Hands and Feet. Surgery, 1939, 5, 1.

82. ABRAMSON, P.D. Clinical Aspects of Arterio Venous Fistulae. Amer. J. Surg., 1939, 44, 429.

83. NEMENOV, M.J. Roentgen Diagnosis of Haemangioma of Long Bones. Radiology, 1939, 33, 465.

84. WERTHEIMER, P. Angiome du Membre Superieur Gauche. Lyon Chir., 1939, 36, 584.

85. TAVERNIER, M. Syndrome de Klippel-Trenaunay. Lyon Chir., 1939, 36, 585.

86. HOMANS, J. Circulatory Diseases of the Extremities, 1939, 264. New York: MacMillan.

87. HOMANS, J. Discussion on paper by Lee and Freeman. Ann. Surg., 1940, 112, 875.

88. COLLEY, R. DAVIES. Cirsoid Aneurysm. Guy's Hosp. Rep., 1940-1, 90, 134.

89. LEE, W.E., and FREEMAN, N.E. Circulatory Disturbances produced by Extensive Angiomata of Lower Extremities associated with Varicose Veins. Ann. Surg., 1940, 112, 960.

90. WRIGHT, L.T. and LOGAN, A.C. Congenital Arterio Venous Aneurysm. Amer. J. Surg., 1940, 48, 658.

91. ECKHOFF, N.L. Cirsoid Aneurysm of Chest Wall. Guy's Hosp. Rep. 1940-1, 90, 141.

92. HORTON, B.T. Hemihypertrophy of Extremities associated with Congenital Arterio Venous Fistula. J. Amer. Med. Ass., 1932, 98, 373.

93. HENCH, P.S. and HORTON, B.T. Extra-Pulmonary Bruits from Arterio Venous Fistula of Intercostal Vessels. Proc. Mayo Clin., 1933, 8, 191.

94. HORTON, B.T. and GHORMLEY, R.K. Congenital Arterio Venous Fistula of Extremities visualised by Arteriography. Proc. Mayo Clin., 1934, 9, 761.

95. HORTON, B.T. and GHORMLEY, R.K. Congenital Arterio Venous Fistula of Extremities visualised by Arteriography. Surg., Gynec., Obstet., 1935, 60, 978.

96 /

96. SMITH, F.L. and HORTON, B.T. Sclerosing Treatment of Congenital Arterio Venous Fistula. Proc. Mayo Clin., 1937, 12, 17.

97. HORTON, B.T. and HEMPSTEAD, B.E. Congenital Arterio Venous Fistula of Middle Ear and External Auditory Meatus. Arch. Oto. Laryng., 1938, 27, 736.

98. WARD, C.E., and HORTON, B.T. Congenital Arterio Venous Communications in Children. J. Paediat., 1940, 16, 746.

99. CRAIG, W. McK. and HORTON, B.T. Diagnosis and Treatment of Vascular Disorders of Extremities. Surg. Clin. N. Amer., 1938, 18, 945.

100. STAUFFER, H.M., ARBUCKLE, R.K. and AEGERTER, E.E. Polyostotic Fibrous Dysplasia with Cutaneous Pigmentation and Congenital Arterio Venous Aneurysms. J. Bone & Joint Surg., 1941, 23, 323.

101. HIRSCHFELD, K. Haemangioma of Hand, involving Phalangeal Bones, with Distinctive Radiological Appearance. Austral. & New Zeal. J. Surg., 1941, 11, 136.

102. WATKINS, A.G. Congenital Arterio-Venous Anastomosis. Brit. Med. J., 1941, 2, 849.

103. LAIRD, E.G. Deep Cavernous Haemangioma of Neck. Amer. J. Surg., 1941, 53, 158.

104. KLEINBERG, S. Angioma of Foot. J. Bone and Joint Surg., 1942, 24, 367.

105. STEINBERG, M.F., GRISHMAN, A., and SUSSMAN, M.L. Angio-Cardiographic Demonstration of Arterio Venous Fistula. Surg., Gynec., Obstet., 1942, 75, 93.

106. TOUROFF, A.S.W. Transthoracic, Transpleural Ligation of First Portion of Left Subclavian Artery. Surgery, 1941, 10, 747.

107. LUKE, J.C. Congenital Arterio Venous Fistula. Canad. Med. Ass. J., 1940, 42, 341.

108. LUKE, J.C. Congenital Arterio Venous Fistulae of Pinna. Canad. Med. Ass. J., 1942, 46, 167.

109. PRATT, G.H. Surgical Treatment of Peripheral Aneurysm. Surg., Gynec., Obstet., 1942, 75, 103.

110. FULTON, M.N. and SOSMAN, M.C. Venous Angiomas of Skeletal Muscle. J. Amer. Med. Ass., 1942, 119, 319.

111 /

111. BOWER, L.E., DITKOWSKY, S.P., KLIEN, B.A., and BRONSTEIN, I.P. Arteriovenous Angioma of Mandible and Retina. Amer. J. Dis. Child., 1942, 64, 1023.

112. SHUMACKER, H.B. Congenital Hypertrophy of Lower Extremity associated with Elephantiasis. Amer. J. Surg., 1942, 58, 258.

113. HALPERT, B. Arterio Venous Communication between Right Coronary Artery and Coronary Sinus. Heart, 1929-31, 15, 129.

114. CALLANDER, C.L. Study of Arterio Venous Fistula. Johns Hopkins Hosp. Rep., 1920, 19, 259.

115. WEBER, F. PARKES. Multiple Hereditary Developmental Angiomata. Lancet, 1907, 2, 160.

116. WEBER, F. PARKES. Haemangiectatic Hypertrophy of Limbs. Brit. J. Child. Dis., 1918, 15, 13.

117. WEBER, F. PARKES. Note on So-called Congenital Varicose Veins. Brit. J. Child. Dis., 1936, 33, 102.

118. WEBER, F. PARKES. Note on Association of Extensive Haemangiomatous Naevus of Skin with Cerebral (Meningeal) Haemangioma. Proc. Roy. Soc. Med., 1928-9, 22, 431.

119. WEBER, F. PARKES. Sturge Kalischer Disease. Brit. Med. J., 1936, 1, 708.

120. FREUDENTHAL, W., ANDERSON, R.G., and WEBER, F. PARKES. Glomus and Glomus Tumour. Brit. J. Derm. and Syph., 1937, 49, 151.

121. BROWN, G.E. Abnormal Arterio Venous Communications diagnosed by Oxygen Content of Blood of Regional Veins. Arch. Surg., 1929, 18 (part 2), 807.

122. LEWIS, SIR T., and DRURY, A.N. Arterio Venous Aneurysm. Heart, 1923, 10, 301.

123a. GOULD, G.M. and PYLE, W.L. Anomalies and Curiosities of Medicine, 1897, p. 778. London: Rebman.

123b. GOULD, G.M. and PYLE, W.L. Ibid. p. 799.

124. FRANKLIN, K.J. A Monograph on Veins, 1938, p. 284 and 331. London: Baillière, Tindall & Cox.

125. NUSSEY, A.M. and MILLER, H.H. Sturge's Disease. Brit. Med. J., 1939, 1, 822.

126 /

126. NORTHFIELD, D.W.C. Angiomatous Malformations of Brain. Guy's Hosp. Rep., 1940-1, 90, 149.

127. BLAND-SUTTON, SIR J. Tumours, Innocent and Malignant, 7th ed., 1922, 167. London: Cassel.

128. HARRIS, R.I. and McDONALD, J.L. Effect of Lumbar Sympathectomy upon Growth of Legs Paralysed by Anterior Poliomyelitis. J. Bone and Joint Surg., 1936, 18, 35.

129. BRASH, J.C. Some Problems in the Growth and Developmental Mechanics of Bone. Edinburgh Med. J., 1934, 41, 305 and 363.

130. McMASTER, P.E. and ROOME, N.W. Effect of Sympathectomy and of Venous Stasis on Bone Repair. J. Bone and Joint Surg., 1934, 16, 365.

131. WU, Y.K. and MILTNER, L.J. A Procedure for Stimulation of Longitudinal Growth of Bone. J. Bone and Joint Surg., 1937, 19, 909.

132. ROWBOTHAM, G.F. Haemangiomata arising in Bones of Skull. Brit. J. Surg., 1942-3, 30, 1.

133. KENNEDY, J.A. and BURWELL, C.S. Measurements of the Circulation in a Patient with Multiple Arterio-Venous Connections. Amer. Heart, J., 1944, 28, 133.

134. BALLANCE, SIR H.A. and SHATTOCK, S.G. Intramedullary Capillary Angioma of Shaft of Humerus. Brit. J. Surg., 1923-4, 11, 622.

135. BUCY, P.C. Pathology of Haemangioma of Bone. Amer. J. Path., 1929, 5, 381.

136. BUCY, P.C. and CAPP, C.S. Primary Haemangioma of Bone. Amer. J. Roentgen, 1930, 23, 1.

137. HITZROT, J.M. Haemangioma Cavernosum of Bone. Ann. Surg., 1917, 65, 476.

138. ANSPACH, W.E. Sun Ray Haemangioma of Bone. J. Amer. Med. Ass., 1937, 108, 617.

139. GESCHICKTER, C.F. and MASERITZ, I.H. Primary Haemangioma involving Bones of Extremities. J. Bone and Joint Surg., 1938, 20, 888.

140. BISGARD, J.D. and HUNT, H.B. Influence of Roentgen Rays and Radium on Epiphyseal Growth of Long Bones. Radiology, 1936, 26, 56.

141. REGEN, E.M. and WILKINS, W.E. Effect of Large Doses of X-Rays on Growth of Young Bone. J. Bone and Joint Surg., 1936, 18, 61.

142 /

142. BARR, J.S., LINGLEY, J.R. and GALL, E.A. Effect of Roentgen Irradiation on Epiphyseal Growth. Amer. J. Roentg. and Radium Ther., 1943, 49, 104.

143. DESAIVE, P. Hypertrophie Congénitale. J. de Radiol. et d'Electrol., 1938, 22, 222.

144. ENGEL, D. Experimental Study of Action of Radium on Developing Bones. Brit. J. Radiol., 1938, 11, 779.

145. PEARSE, H.E., and MORTON, J.J. Stimulation of Bone Growth by Venous Stasis. J. Bone and Joint Surg., 1930, 12, 97.

146. PHEMISTER, D.B. Operative Arrestment of Longitudinal Growth of Bones in Treatment of Deformities. J. Bone and Joint Surg., 1933, 15, 1.

147. HARVEY, W.F., DAWSON, E.K. and INNES, J.R.M. Debatable Tumours in Human and Animal Pathology - 1X. Endothelioma. Edinburgh Med. J., 1940, 47, 513.

148. MACKEY, W.A. and LENDRUM, A.C. Three Cases of Glomangioma or Angioneuromyoma. Brit. J. Surg., 1936-7, 24, 208.

149. LENDRUM, A.C., and MACKEY, W.A. Glomangioma. Brit. Med. J., 1939, 2, 676.

150. MASSON, P. Le Glomus neuromyo-artériel des régions tactiles et ses tumeurs. Lyon Chir., 1924, 21, 257.

151. WEIDMAN, F.D. and WISE, F. Multiple Glomus Tumours. Arch. Derm. and Syph., 1937, 35, 414.

152. STOUT, A.P. Tumours of the Neuromyo-Arterial Glomus. Amer. J. Cancer, 1935, 24, 255.

153. BAILEY, O.T. The Cutaneous Glomus and its Tumours. Amer. J. Path., 1935, 11, 915.

154. GREIG, D.M. Subcutaneous Glomal Tumours. Edinburgh Med. J., 1928, 35, 565.

155. LEWIS, D. de W., and GESCHICKTER, C.F. Glomus Tumours. J. Amer. Med. Ass., 1935, 105, 775.

156. RAISMAN, V. and MAYER, L. Tumour of the Neuromyo-Arterial Glomus. Arch. Surg., 1935, 30, 911.

157. MASON, M.L. and WEIL, A. Tumour of a Subcutaneous Glomus. Surg., Gynec., Obstet., 1934, 58, 807.

158. ADAIR, F.E. Glomus Tumour. Amer. J. Surg., 1934, 25, 1.

159 /

159. POPOFF, N.W. The Digital Vascular System. Arch. Path., 1934, 18, 295.

160. WOOLLARD, H.H. Development of Arteries in Fore Limb of Pig. Contributions to Embryology, Carnegie Institute, 1922, 14, 139.

161. SABIN, F. Development of Primitive Blood Vessels. Contributions to Embryology, Carnegie Institute, 1917-18, 6-7, 61.

162. KROGH, A. Anatomy and Physiology of Capillaries, 1929, 100. Yale University Press.

163a. MacCALLUM, W.G. Text Book of Pathology, 7th ed. 1940, pp. 348, 1077. Philadelphia: Saunders.

163b. MacCALLUM, W.G. Ibid p. 182.

164. WATSON, W.L. and McCARTHY, W.D. Blood and Lymph Vessel Tumours. Surg., Gynec., Obstet., 1940, 71, 569.

165. JENKINS, H.P. and DELANEY, P.A. Benign Angiomatous Tumours of Skeletal Muscles. Surg., Gynec., Obstet., 1932, 55, 464.

166. MUIR, SIR R. Text Book of Pathology, 4th ed., 1936, 222. London: Arnold.

167. ADAMI, J.G. Principles of Pathology, 1909, Vol. 1, p. 748. London: Henry Frowde, Hodder and Stoughton.

168. EWING, J. Neoplastic Diseases, 4th ed., 1940, 249. Philadelphia: Saunders.

169. JAFFÉ, R.H. Multiple Haemangiomas of the Skin and of the Internal Organs. Arch. Path., 1929, 7, 44.

170. CUSHING, H. and BAILEY, P. Tumours arising from the Blood Vessels of the Brain, 1928. London: Baillière, Tindall and Cox.

171. OUGHTERSON, A.W. and TENNANT, R. Angiomatous Tumours of Hands and Feet. Surgery, 1939, 5, 73.

172. MASON, M.L. Tumours of the Hand. Surg., Gynec., Obstet., 1937, 64, 129.

173. PARSONS, L.G. and EBBS, J.H. Generalised Angiomatosis presenting Clinical Characteristics of Storage Reticulosis. Arch. Dis. Child., 1940, 15, 129.

174 /

174. ROBINSON, J.M. and CASTLEMAN, B. Benign Metastasising Haemangioma. Ann. Surg., 1936, 104, 453.

175. FRASER, SIR J. Haemangioma Group of Endotheliomata. Brit. J. Surg., 1919-20, 7, 335.

176. SHAW, J.J.M. Haemangioma. Lancet, 1928, 1, 69.

177. BALLANCE, SIR C.A. Discussion in Medical Society of London. Lancet, 1906, 2, 1512.

178. PATEY, D.H. Arterio Venous Aneurysm of Scalp. Brit. J. Surg., 1941-2, 29, 290.

179. FITZWILLIAMS, D.C.L. Etiology of Naevi. Brit. Med. J., 1911, 2, 489.

180. HOLMAN, E. Clinical and Experimental Observations on Arterio Venous Fistula. Ann. Surg., 1940, 112, 840.

181. EDWARDS, E.A. and EDWARDS, J.E. Effect of Thrombo Phlebitis on Venous Valve. Surg., Gynec., Obstet., 1937, 65, 310.

182. EDWARDS, E.A. Status of Vasography. New Engl. J. Med., 1933, 209, 1337.

183. PETERS, J.P. and VAN SLYKE, D.D. Quantitative Clinical Chemistry, 1932, Vol. II, 321. London: Baillière, Tindall and Cox.

184. ALLEN, E.V. and CAMP, J.D. Arteriography. J. Amer. Med. Ass., 1935, 104, 618.

185. Council of Pharmacy and Chemistry of American Medical Association.
Report on Thorotrast. J. Amer. Med. Ass., 1932, 99, 2183.

186. Editorial: Potential Hazards of Diagnostic Use of Thorium Dioxide. J. Amer. Med. Ass., 1937, 108, 1656.

187. BIRD, C.E. Use in Arteriography of Substitutes for Colloidal Thorium Dioxide. J. Amer. Med. Ass., 1937, 109, 1686.

188. POMERANZ, M.M. and TUNICK, I.S. Visualisation and Obliteration of Angiomata by Radio-opaque Solutions. Ann. Surg., 1941, 114, 1050.

189. ROBB, G.P. and STEINBERG, I. Practical Method of Visualisation of Chambers of Heart, Pulmonary Circulation and Great Blood Vessels in Man. J. Clin. Invest., 1938, 17, 507.

190 /

190. FLEMING, A.J. and CHASE, W.H. Effects of Administration of Thorium Dioxide. Surg., Gynec., Obstet., 1936, 63, 145.

191. TREVES, SIR F. Case of Pulsating Tumour of Head. Brit. Med. J., 1886, 2, 721.

192. GRANT, R.T. Portable Thermo-Electric Couple for Measuring Skin Temperature. Guy's Hosp. Rep., 1935, 85, 209.

193. CAMPBELL, W.C. Congenital Hypertrophy. Surg., Gynec., Obstet., 1923, 36, 699.

194. BANKART, A.S.B. Hemihypertrophy. Proc. Roy. Soc. Med., 1915-16, Vol. 9, Part 1, Sect. Dis. Child., p. 77.

195. HUTCHISON, SIR R. Case of Hemihypertrophy. Proc. Roy. Soc. Med., 1915-16, Vol. 9, Part 1, Sect. Dis. Child., p. 66.

196. KEITH, SIR A. Human Embryology and Morphology, 5th ed., 1933, 379. London: Arnold.

197. CUNNINGHAM, D.J. Text Book of Anatomy, 8th ed., 1943, 81. Oxford Medical Publications.

198. GREIG, D.M. Clinical Observations on Surgical Pathology of Bone, 1931,1,Edinburgh: Oliver and Boyd.

199. JONES, R.W. and ROBERTS, R.E. Calcification, Decalcification and Ossification. Brit. J. Surg., 1933-4, 21, 461.

200. FALCONER, M.A., COPE, C.L. and ROBB-SMITH, A.H.T. Fibrous Dysplasia of Bone with Endocrine Disorders and Cutaneous Pigmentation (Albright's Disease). Quart. J. Med. (New Series), 1942, 35,121.

201. CARLETON, A., ELKINGTON, J. St.C., GREENFIELD, J.G. and ROBB-SMITH, A.H.T. Maffucci's Syndrome. (Dyschondroplasia with Haemangiomata). Quart. J. Med. (New Series), 1942, 35, 203.

202. SHENNAN, T. Histologically Non Malignant Angioma with Numerous Metastases. J. Path. Bact., 1914, 19, 139.

203. ACKERMANN, A.J. and HART, M.S. Multiple Primary Haemangioma of Bones of Extremity. Amer. J. Roentg., 1942, 48, 47.

204. BERGSTRAND, H. Multiple Glomic Tumours. Amer. J. Cancer, 1937, 29, 470.

205/

205. GRANT, R.T. Observations on Direct Communications between Arteries and Veins in the Rabbit's Ear. Heart, 1930, 15, 281.

206. MURRAY, M.R. and STOUT, A.P. Glomus Tumour. Amer. J. Path., 1942, 18, 183.

207. STOUT, A.P. and MURRAY, M.R. Haemangiopericytoma. Ann. Surg., 1942, 116, 26.

208. MATAS, R. Keen's Surgery, 1909, Vol. 5, p. 290. Philadelphia: Saunders.

209. MAKINS, SIR G.H. On Gunshot Injuries to the Blood Vessels, 1919, 68. Bristol: Wright.

210. BAILEY, W. and KISKADDEN, W.S. Treatment of Haemangiomata. Radiology, 1942, 38, 552.

211. LIGHT, S.E. Injection Treatment of Cavernous Haemangioma. Arch. Derm. and Syph., 1931, 24,992.

212. KAPLAN, I.I. Haemangioma of Elbow successfully treated with Radium at an Early Age. Amer. J. Dis. Child., 1943, 65, 785.

213. POHLE, E.A. and McANENY, J.B. Radium Treatment of Vascular Naevi. Amer. J. Roentg., 1940, 44, 747.

214. BERSON, M.I. Surgical Removal of Haemangioma of Face. Amer. J. Surg., 1941, 51, 362.

215. SEARBY, H. Cirsoid Aneurysm of Scalp. Austral. and New Zeal. J. Surg., 1931, 1, 209.

216. KERR, H.D. Irradiation Treatment of Cavernous Haemangioma. Radiology, 1942, 39, 4.

217. ABBOTT, L.C. Operative Lengthening of Tibia and Fibula. J. Bone and Joint Surg., 1927, 9, 128.

218. EALING, M.I. Haemangioma of Arm Causing Delay in Delivery and Neonatal Death. J. Obstet. Gynec., Brit. Emp., 1943, 50, 144.

219. FINLEY, R.K. and SHAFFER, J.M. Congenital Arterio Venous Aneurysm. Ohio State Med. J., 1943, 39,334.

220. KULCHAR, G.V. Benign and Malignant Tumours of Foot. J. Amer. Med. Ass., 1944, 124, 761.

221. ELMSLIE, R.C. Robert Jones Birthday Volume, 1928, 153. Oxford University Press.

222./

222. LOVE, J.G. and HORTON, B.T. Paralysis of Ulnar Nerve due to Arterio-Venous Fistula. Proc. Mayo Clin., 1944, 19, 441.

223. LEARMONTH, J.R. Arteriography of Peripheral Vessels. Lancet, 1944, 2, 745.

224. SLEPYAN, A.H. Multiple Painful and Painless Glomus Tumours. Arch. Derm. and Syph., 1944, 50, 179.

225. ZONDEK, H. Diseases of the Endocrine Glands, 2nd English ed., 1944, pp. 18, 47 and 335. London: Arnold.

ACKNOWLEDGMENTS.

I wish to express my gratitude to Professor J.R. Learmonth, for permitting me to examine and to investigate four of his own cases, Cases Three, Four, Eleven and Twelve, for affording me the opportunity of witnessing and taking part in his operations and for making available to me the results of several investigations. The late Mr. W.A. Cochrane kindly allowed me access to his records of Case Five. Case Two was a private patient of Mr. J.W. Heekes, of the Royal Hospital, Richmond, Surrey, and I am indebted to him for having been able to examine her and for sending me copies of the X-Ray films.

To others I wish to extend my thanks for their invaluable help and for their courtesy in making several very specialised investigations.

The X-Ray examinations, with the above exception, and also the radiotherapy, were carried out under the charge of Dr. R. McWhirter.

The skin temperature tests were carried out by Dr. R.L. Richards in Cases Three, Four, Eight and Eleven, and by Dr. A.E. Claireaux in Case One.

The pathological and histological examinations were made by Dr. R.F. Ogilvie, Dr. W. Blackwood and Dr. W. Forbes.

The estimations of the oxygen content of the venous blood were performed by Miss E. Gilchrist, and the estimations of the blood volume by Miss M.H. Roscoe.

The photography was the work of Dr. D. Aitken, Mr. T.C. Dodds, Mr. H. Martin, Mr. F.W. Pettigrew, Mr. D. Smith and Messrs A.H. Baird. Fig. 65 was a tracing by Mr. C. Shepley from a photograph.